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LATE RESULTS OF DIRECT SURGERY OF THE AORTIC BIFURCATION AND ITS MAJOR BRANCHES

BY

F. B. COCKETT, M.S., F.R.C.S. AND A. G. NORMAN, F.R.C.S.

Consultant Surgeon *Senior Surgical Registrar*

St. Thomas's Hospital, London

[WITH SPECIAL PLATE]

The replacement of the terminal aorta and its main branches by stored homografts for obliterative disease or aneurysm is an operation which is being performed with increasing frequency. More recently (Hufnagel, 1955; Rob, 1956; Owen, 1956; Kinmonth *et al.*, 1955) these vessels have been successfully replaced by plastic artificial arteries made of "orlon," "nylon," or polyvinyl sponge, particularly in cases of aneurysm. After new and technically successful procedures such as these have been practised for a number of years it is well to review and take stock of the results carefully, for it is only as the long-term follow-up results begin to emerge that a true perspective can be obtained. Although large numbers of these operations have been reported from various centres (Linton, 1956; Rob *et al.*, 1956; DeBakey *et al.*, 1955), so far few detailed follow-up studies over an adequate period of time on individual series have appeared. In our experience any follow-up of less than one year is inadequate for assessing results in this type of surgery. It is during the first year that delayed occlusion of anastomosis is most likely to take place. It is only on such figures, combined with an estimate of the mortality and morbidity, that the indications for these procedures can be finally assessed.

Thus the purpose of this paper is threefold: (1) to describe our experience with 30 patients in whom reconstruction or replacement of the aortic bifurcation or one of its major branches has been carried out, and to describe the follow-up results to date; (2) to enumerate some of the lessons we have learned on the technique of doing these operations and handling the patients; and (3) to present some conclusions as to the long-term results which may be expected, and therefore on the indications for operative treatment. We have confined this paper to our experiences with the large arteries, ranging from the aorta to the common femoral. Our experiences with the commoner femoral-artery occlusions will be the subject of a further paper.

Clinical Material

Of the 30 patients, 26 came to operation because of an arteriosclerotic thrombosis of the aortic bifurcation or one or other common or external iliac artery; 4 patients had an aneurysm of the aorta.

The symptoms caused by the high arterial occlusions depend on the situation and degree of occlusion and the age of the patient and whether or not there is further arterial disease in the limb lower down. But, in general, there are three grades of severity of symptoms.

Grade I: Whole-leg and Buttock Claudication.—After a certain amount of exercise the patient complains of an aching pain which may start either in the buttocks or in the calf; but unless the exercise ceases it rapidly spreads to the thigh and the patient is pulled up by a severe ache and feeling of uselessness in his buttocks, thighs, and calf. The pain disappears after a minute or so standing still. This typical spread of exercise pain in buttocks, thigh, and leg is often described by the patient as rheumatism or lumbago, or just as a general ache and feeling of uselessness. Severe pain or cramp is seldom complained of, and so the symptoms are often misinterpreted. Several of our patients with whole-leg and buttock claudication have had months or years of physiotherapy for lumbago and rheumatism before the true nature of the pain was elucidated by finding that one or other femoral pulse was missing.

Grade II: Cold Leg.—With a local occlusion of the bifurcation or one or other common iliac artery, whole-leg and buttock claudication may be the only symptom. But if the thrombosis is a little more widespread, and the patient older so that the collateral circulation is not so good, then he may also complain of a persistent cold foot or feet and sometimes numbness in the foot; at this stage, too, some wasting of muscles may appear.

Grade III: Incipient Gangrene.—Finally, with a localized occlusion of a major branch of the aorta in addition to arterial disease lower down in the limb (such as local femoral or popliteal occlusion or thrombosis) the severe ischaemic symptoms and signs appear. These are rest pain, robbing the patient of his sleep at night, with numbness and coldness of the toes and foot. Rubor on dependency is seen, and impending gangrene of one or more toes may be present.

In all the cases of abdominal aneurysm the symptom necessitating operation was pain.

Methods

The surgical methods used for dealing with these thrombosed arterial segments or aneurysms have been of three kinds. (I) Replacement or by-passing the occluded segment with a stored arterial homograft. Our "artery bank" and method of storage are exactly the same as those introduced into this country in 1950 by Eastcott (Eastcott, 1953). This method of reconstruction was used in 18 cases. (II) Replacement by a plastic "artificial artery," either of polyvinyl sponge (three cases) or of orlon (three cases). (III) "Disobliteration" or "endarterectomy" of an occluded segment. This method, originally described by Dos Santos (1947) and Reboul and Laubry (1950), involves opening the artery and removing the thrombus from inside. Its ideal application is to a large artery, with a short localized occlusion with good normal artery on either side. This method was used in six cases.

We propose now to tabulate our results under these three headings.

Series I: Replacement or "By-passing" of the Occluded Segment with a Stored Arterial Homograft

Table I gives details of results and length of follow-up in this group of 18 patients, and the accompanying diagrams record the type of operative procedure in each case. In all cases a deep frozen homograft collected and preserved in our "artery bank" after the method described by Eastcott (1953) was used. In the earlier cases the grafts were collected with full sterile precautions and were not subjected to further sterilizing. Since late 1955, however, all our grafts have been sterilized by half an hour's immersion in ethylene dioxide (Hufnagel *et al.*, 1954). We have, however, found that in spite of this no relaxation of the sterile precautions when taking the graft can be allowed. Also, perhaps even more important, the donor must not have been dead more than eight to ten hours before the graft is taken; with grafts removed later than this one cannot be absolutely sure of sterility, as the process of post-mortem autolysis seems to be associated with a rapid spread of bacteria throughout the body, and they may be found within the vasa vasorum of the graft and thus not reached by a surface sterilisant. This question of the absolute sterility of grafts is of the utmost importance—as the presence of staphylococci on a suture line will lead to late leakage and rupture. There are two cases in this series (Nos. 10 and 13) in which late leakage and rupture of an anastomosis was probably due to this factor. It is possible that sterilization of the grafts by *x* rays is the most satisfactory method (Meeker and Gross, 1951), and this is under investigation at present.

Indications for Operation

In nine of the patients the indication for treatment was severe claudication in one or both legs. In all cases the claudication was getting steadily worse and was causing the patient considerable anxiety, and in about half of them it was actively interfering with their work. In the other nine cases the ischaemic symptoms were more severe—ischaemic numbness and coldness and rest pain, with in three cases minor gangrene. These patients were all facing loss of a limb in the near future and therefore operation was undertaken to save the limb.

TABLE I.—*Series I: Replacement or By-passing with Stored Homograft*

Case No.	Sex and Age	Date of Operation	Procedure	Result	Follow-up	Remarks
1	M 50	10/2/53	Short-segment end-to-end graft of right *common* femoral, just at inguinal ligament level	Full return of pulses	4 yrs. 5 mths.	Graft functioning perfectly 4 yrs. 5 mths. after operation. Patient symptomless
2	M 57	19/2/53	Right common iliac to right external iliac, end-to-end anastomosis	Full return of pulses	4 yrs. 2 mths.	Aortic bifurcation above graft occluded 1 yr. after operation. Return of claudication to right leg, with some rest pain. (Has angina)
3	M 47	19/5/53	Left common iliac artery resection; end-to-end graft	Return of pulses	3 yrs. 1 mth.	Complete relief of claudication. Died of hypertension 3 yrs. 1 mth. after operation. At necropsy graft patent and indistinguishable from normal artery
4	M 60	15/2/54	Aortic bifurcation resected: end-to-side on right external iliac; end-to-end on left internal iliac	Full return of pulses	3 yrs. 2 mths.	Left end-to-end anastomosis occluded about 8 mths. after operation. Right end-to-side anastomosis still functioning. Has angina but is still at work
5	M 61	31/1/55	Aortic bifurcation resected: end-to-side to right femoral artery; end-to-side to left external iliac	Full return of pulses	2 yrs. 6 mths.	Perfect result maintained. All pulses present. Symptomless warm lower extremities
6	F 65	20/3/55	Right common iliac near bifurcation of aorta to right external iliac	Failure. Pulses did not return	2 yrs. 4 mths.	Lost right leg but otherwise well. Right leg pregangrenous and due for amputation unless graft could save it
7	M 46	17/5/55	Left common iliac (close to bifurcation) to left superficial femoral in leg (end-to-side)	Graft functioned well	2 yrs. 3 mths.	Severe rest pain with ischaemic ulcer of ankle. Graft relieved pain, healed ulcer, and averted amputation; is still patent
8	M 49	18/7/55	Bifurcation graft. Distal ends, end-to-side anastomosis on right side, end-to-end on left	Full return of pulses	2 yrs.	Complete relief of severe claudication. At full work
9	M 48	3/11/55	By-pass graft from right common iliac to common femoral	Graft functioned well	1 yr. 9 mths.	Graft averted major amputation; two toes only lost. Doing sedentary work
10	M 56	6/4/55	Aortic bifurcation graft. Distal limbs, end-to-side anastomoses	Full return of pulses	2 yrs. 3 mths.	Severe staphylococcal enteritis developed after operation. Later an infective false aneurysm appeared from leakage at right external iliac anastomosis. This had to be destroyed, and as a result patient lost right leg. Other limb of graft still functioning well
11	M 57	5/7/56	Aortic bifurcation graft. Distal limbs, end-to-side anastomoses	Full return of pulses to left leg; right leg cold and dead	1 yr.	Complete recovery of left leg (which was the bad one) maintained. Right leg amputated above knee because of a popliteal embolus sustained at operation
12	M 49	13/8/56	External iliac to common femoral (end-to-end)	Full return of pulses	1 yr.	Disabling claudication of left leg, causing loss of work. Now back at work with no claudication
13	M 43	26/11/55	Aortic bifurcation up to renal arteries. Distal limbs end-to-side	Full return of pulses	Died suddenly 1 wk. after discharge from hospital	Disabling claudication. Operative result perfect; discharged fit and symptom-free. Died suddenly 1 wk. after discharge after attack of acute abdominal pain. Probably ruptured aortic anastomosis due to sepsis, as *Staph. aureus* grown in broth culture of piece of graft inserted at operation
14	M 53	19/11/56	Aortic bifurcation: right limb end-to-side; left limb end-to-end	Full return of pulses below graft	9 mths.	Severely handicapped with threatened gangrene of right leg and severe claudication. 5 mths. after operation left end-to-end anastomosis occluded with return of claudication in left leg. Right leg maintains full improvement. Underwent sympathectomy and soleus denervation for left leg, with considerable improvement. Now back at sedentary type of job
15	M 48	5/12/56	Aortic bifurcation. Right limb end-to-side to right superficial femoral; left limb end-to-side left common femoral (both below inguinal ligament)	Full return of pulses	8 mths.	Disabling claudication. Had previously had a polyvinyl sponge graft inserted (elsewhere) which had thrombosed. At present operation thrombosed polyvinyl graft removed and homograft inserted. Now back at full work
16	M 53	9/1/57	By-pass graft from left common iliac to left common femoral	Full return of pulses	Died 2 wks. after operation	Disabling claudication of left leg. Operation technically very successful. However, chronic paralytic ileus followed by chest complication developed. Went steadily downhill and died 2 wks. after operation. At necropsy chronic paralytic ileus and infarction of lower lobes of both lungs found. Graft functioning perfectly. No satisfactory explanation of death
17	F 43	8/5/57	Aortic bifurcation. Right end-to-side. Left end-to-end (good fit)	Full return of pulses	4 mths.	Increasing claudication of whole lower limbs which was gradually disabling her. Full return of pulses and completely satisfactory result maintained during relatively short follow-up
18	F 57	1/7/57	Aortic bifurcation. Both ends, end-to-side to external iliacs	Full return of femoral pulses	2 mths.	Continuous rest pain in left leg, preventing sleep; also claudication at about 20 yd. and cold, numb feet. After operation immediate relief from rest pain and warm extremities

Mortality

In this group of 18 cases there were two deaths. The patient in Case 13, after a technically very successful operation, had an uninterrupted convalescence and was discharged symptom-free and apyrexial three weeks after operation. One week later he was seized with acute abdominal pain and died suddenly that same afternoon. No necropsy was performed. In this case, although ordinary bacterial culture of a piece of the graft taken at the operation, by wiping it on an agar plate, was sterile, culture in broth gave a growth of *Staphylococcus aureus*. It is our belief that this case represents a late rupture of the anastomotic line due to sepsis in the graft.

The patient in Case 16 died with progressive paralytic ileus, massive infarction of both lower lobes of the lungs, and progressive renal failure. Again this was a technically successful and smooth operation, and the ultimate cause of death was never satisfactorily fathomed.

The rest of the patients (except Case 3) are alive and well, and most of them are working at the time of writing.

Morbidity and Complications

These are all fairly major operations on a group of patients with arteriosclerosis and in the 45–65 age group. The incidence of major complications has been very low. A certain amount of post-operative ileus is an inseparable accompaniment of an extensive retroperitoneal dissection, and continuous suction and an intravenous drip for two to four days have usually been necessary. Blood transfusion has been required in all cases.

In one case (Case 6) the graft was a failure owing to an unsatisfactory technical anastomosis at the aorta, where a large plaque interfered with it. In the light of later experience this could have been avoided by either resecting the whole bifurcation or simply doing a thrombendarterectomy of the occluded segment. However, this graft was not functioning at the end of the operation and the patient lost her right leg. This operation was undertaken to avert an amputation, and its failure meant the loss of her "bad" leg only.

A major complication occurred in two cases. In Case 10 a fulminating staphylococcal enteritis developed the day after operation from which the patient nearly died. He survived this with massive saline infusions and antibiotic therapy. About six weeks after operation, however, it became apparent that he had a false aneurysm due to leakage at the site of the anastomosis of the right limb of the aortic bifurcation graft to the right external iliac artery. This anastomosis had to be destroyed completely at a subsequent operation, and as a result his right leg had to be amputated. However, he recovered from all this; his left anastomosis is still working and he is back in active life again with an artificial limb.

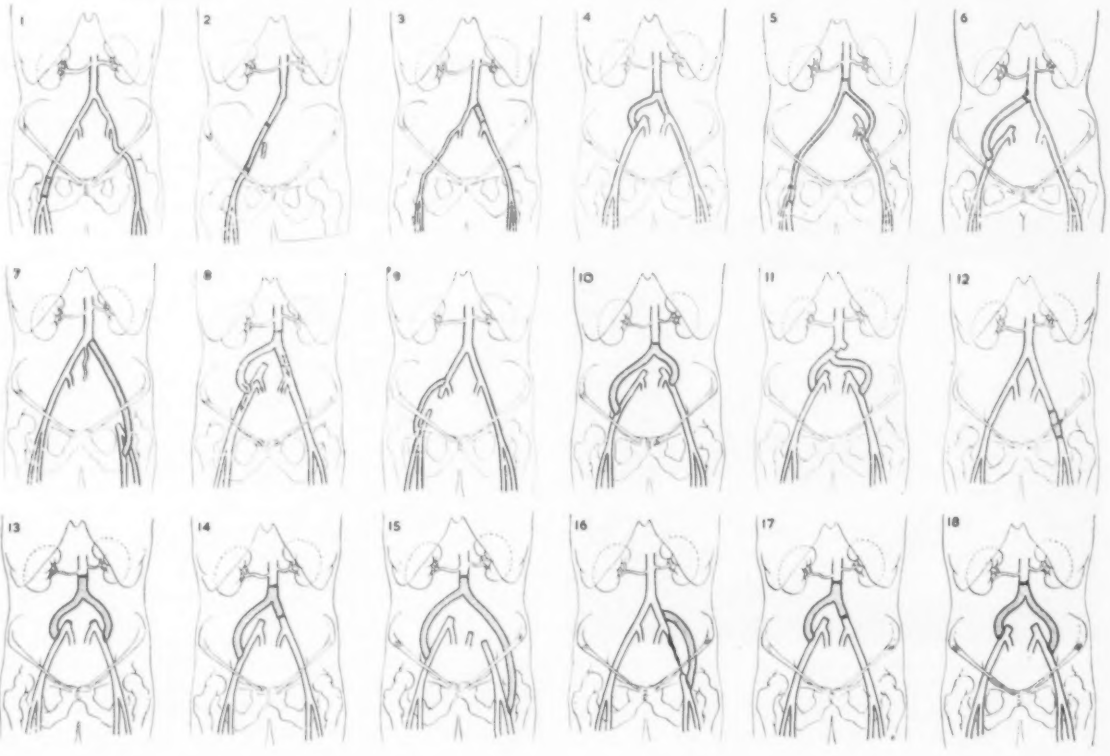
Case 11 represents the worst complication encountered. Here operation was undertaken to avert amputation of the left leg. Unfortunately, at operation an embolus from the site of the graft was allowed to slip unnoticed into the right popliteal artery, causing gangrene and necessitating loss of the right leg. The net result was that the patient's "bad" leg recovered completely and is in full use with all pulses present to-day, but he lost what was his "good" leg.

This complication of an embolus slipping down into the distal arteries after release of the clamps on the aorta must be guarded against. Now we never complete an arterial anastomosis before opening the proximal clamp and "flushing out" any clot which may be in the vessel proximal to the clamp.

Technique of Inserting Grafts

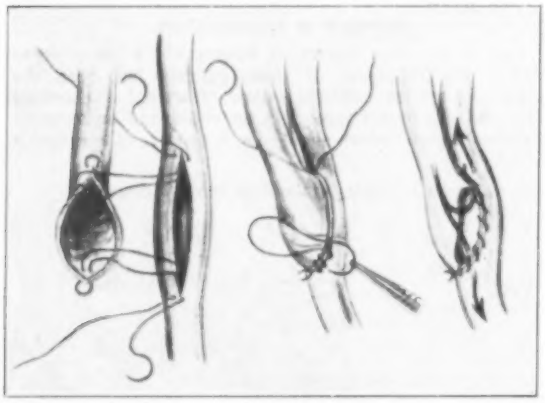
One of the most interesting lessons which has emerged during the follow-up of these patients has been the superiority of the end-to-side type of arterial anastomosis over the end-to-end type. In an end-to end anastomosis between a graft (which should be in good condition) and a

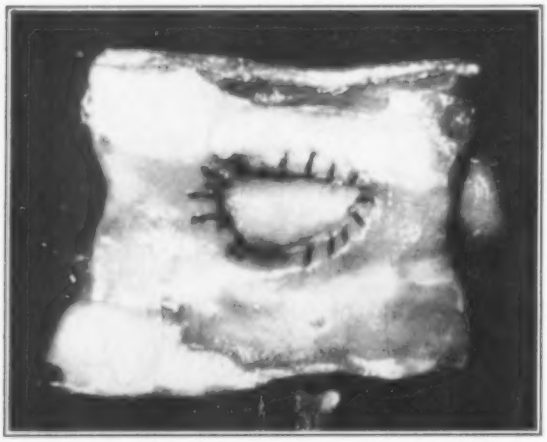
Diagrammatic Representation of Operative Procedures in Series I (Table I) (Numbers refer to cases)



host artery (which is usually arteriosclerotic to some degree) a certain amount of irregularity and constriction is almost bound to occur. Moreover, there may be some disparity in size between host and graft. These factors, in our experience, lead to irregularity of flow over the site of the suture line and the gradual deposition of a platelet thrombus, which narrows and finally occludes the site of anastomosis. Thus late occlusion (after three to nine months) has been the main cause of failure of end-to-end anastomosis of arteries. The incidence of late occlusion is less in very large vessels such as the aorta or common iliac arteries. But in order to ensure that an end-to-end arterial anastomosis shall remain patent for many years the following conditions must be met: (1) the arteries to be anastomosed must be of exactly the same size—that is, they must be a perfect fit; (2) the suturing must be done with technical skill so that the suture line is not constricted in any way—this is difficult; (3) the "normal" graft artery must not be sutured to a thickened or irregular segment of host artery—this inevitably leads to irregularity of the suture line, obstruction of smooth flow, and, therefore, late thrombosis; and (4) the arteries must be sutured under the right tension, so that when the clamps are removed the anastomosis is not suddenly distorted.

Now, in handling arteriosclerotic arteries it is only rarely possible to fulfil all these requirements consistently, particularly Nos. 1 and 3. Therefore, early in 1954 one of us (F. B. C.) started to perform the smaller arterial anastomoses by an end-to-side technique (see Fig.). After a time it became apparent that this type of anastomosis was less prone to late thrombosis than the end-to-end type. This, we believe, is mainly due to the fact that a much larger opening between the two arteries to be sutured can be obtained by this technique. The feasibility of using this type of anastomosis has already been shown by Kunlin using vein grafts (Kunlin, 1949, 1951).





Technique of end-to-side large-lumen anastomosis. Photograph is of an end-to-side anastomosis between a graft and common iliac artery, removed from a patient who died from other causes ten days after implantation (Case 16, Table I). Note complete absence of thrombus round suture line.

In the present series comparison of the late results of end-to-end and end-to-side anastomoses is instructive. Cases 2 and 14 (see Table I) are of particular interest. In both of these the arteries were in very bad condition; both had an aortic bifurcation graft inserted with the right-hand limb sutured end-to-side into the right external iliac artery and the left-hand limb sutured end-to-end on to the left common iliac artery. In both cases the end-to-end anastomosis became occluded after eight months and five months respectively. In both cases the right end-to-side anastomosis remains patent after three years and ten months respectively.

All the end-to-end anastomoses in this series which have remained patent over two years or more have been between arteries of large size; the artery at the site of the anastomosis has not been diseased; and a "good fit" between graft and host artery has been achieved. There have been ten end-to-end anastomoses between major arteries followed up for one to three years, with two late occlusions; and nine end-to-side anastomoses (all on more diseased segments of artery and on artery of smaller size than the former group) followed up for one to three years with no incidence of late occlusion. In fact, in the whole of the series there has not yet been a case of delayed occlusion of an end-to-side type of anastomosis.

Our experience with grafting of the smaller arteries such as the superficial femoral artery has amply confirmed the superiority of the end-to-side type of anastomosis. The results of other workers, notably Linton (1955), Crawford and DeBakey (1955), and Martin and Gaylis (1957), have also confirmed this.

A further and very important advantage of this technique is that once the aortic anastomosis has been completed the two ends of the bifurcation graft can be taken down well beyond the diseased area without further dissection and disturbance of existing collateral vessels, and implanted into as healthy a portion of artery as can be found lower down. Fig. 1 (Special Plate) shows the pre- and post-operative aortograms of Case 5 (Table I), in which the right-hand limb has been brought below the inguinal ligament and sutured end to side to the right femoral artery. Long areas of severely diseased artery can be by-passed in this way.

General Assessment of Results in this Series

In this group of 18 patients two have died in the early post-operative period as a direct result of the operation. Of the remaining 16, there has been a serious complication resulting in loss of a limb in three cases. (In two of these amputation would have been necessary even if no operation had been undertaken.) The remaining 13 cases have been successful in varying degrees. In one patient (Case 4) symptoms returned after one year owing to a fresh occlusion of the aorta above the graft. This patient illustrated the need for being thoroughly radical when dealing with arteriosclerotic disease which is widespread—he should have had an aortic bifurcation graft. In two other cases there has been late occlusion of one of the end-to-end anastomoses, but in both there is still improvement due to the patency of the other anastomosis. The remaining ten patients have had very good results. Three patients in particular have been rescued from amputation by the operation. These good results have been maintained for between two and three years in six of these cases.

Considering the uniformly serious and progressive nature of the arteriosclerotic occlusive disease for which these operations were undertaken these results are very encouraging. Nearly all the patients had nothing to look forward to but steadily progressive disablement with eventual loss of

one or both limbs. These ten good results may therefore be looked upon as a salvage from certain serious disability. Moreover, as the tricks of technique and judgment have been learned the risk and complication rate has steadily decreased. It is also noteworthy that nine of these patients were under 50 and facing serious curtailment of their earning capacity during the most responsible period of their lives. The oldest patient in the series was 65. Two of the patients had angina (Cases 2 and 4). One only had hypertension (Case 1).

Series II: Replacement with Plastic Prosthesis (Polyvinyl Sponge) or Orlon Cloth

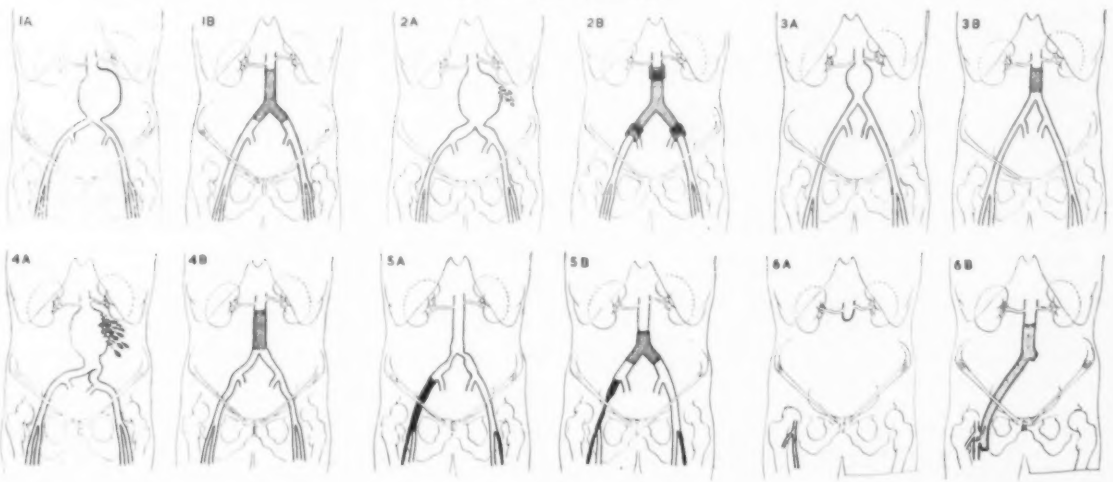
From Table II it will be seen that four of these six patients had an aneurysm of the aorta. The indication for operation here is increasing pain, which usually foretells rupture in the near future. One case (Case 2) had a leakage some time before operation. In another (Case 4) leakage was actually taking place when operation was done as an emergency. One of the technical problems of excising abdominal aneurysms is that the aortic ends which are left after excision of the aneurysm are very large; in this situation an orlon tube made to fit the large aorta is the best prosthesis in our experience (Special Plate, Fig. 2). Orlon tubes have the advantages that they are easy to make, easy to sew and handle, and are incorporated in the body tissues after implantation (Hufnagel, 1955; Kinmonth *et al.*, 1955).

One case of aneurysm and two cases of aortic thrombosis had a compressed polyvinyl sponge tube inserted (Owen, 1956). One of these latter showed late thrombosis (Case 6). Although in the other two cases of replacement by polyvinyl sponge the prostheses are still patent, we have now given up the use of this material for the following reasons: (1) it is treated more like a foreign body by the tissues—it is encapsulated and walled off, and fibrous tissue does not

TABLE II.—*Series II: Replacement with Plastic Prosthesis (Polyvinyl Sponge) or Orlon Cloth*

Case No.	Sex and Age	Date of Operation	Procedure	Result	Length of Follow-up	Remarks
1	M 81	1.10.56	Replacement of aorta between renal arteries and iliacs; orlon fabric tube	All pulses returned to lower limbs	7 days; then died from pulmonary embolus	Had an abdominal aneurysm which was enlarging and giving pain. Came through operation very well and was quite fit, but died suddenly on 7th day from massive pulmonary embolus
2	M 64	17.3.56	Replacement of aorta between renals and iliacs; polyvinyl sponge prosthesis	All pulses returned to lower limbs	1 yr. 4 mths. (graft patent)	Leak from large abdominal aneurysm about 2 mths. before operation; was getting pain. Operation prolonged and difficult; cerebral thrombosis developed in post-operative period. This gradually improved, however. Now back at light work, and apart from slight residual aphasia and weakness of right hand is in good shape
3	M 69	8.10.56	Replacement of aorta between renals and iliacs; orlon fabric tube	Complete return of all pulses	10 mths.	Quite small aneurysm of aorta, but caused continuous throbbing pain. This symptom lost after operation and at time of writing patient is well and fit
4	M 68	17.4.57	Replacement of aorta between renals and iliacs; orlon fabric tube	Complete return of pulses	4 mths.	Admitted as emergency with leaking abdominal aneurysm. Pain and large solid mass in left flank with some skin bruising. Operation undertaken as emergency. Smooth convalescence and left hospital 3 wks. later, still well
5	M 66	8.3.56	Polyvinyl sponge prosthesis from aorta to right femoral artery	Complete return of pulses	Graft closed 5 mths. later. Died 9 mths. after operation	Obliteration of aorta up to renal arteries. Lost left leg (above knee) and getting severe rest pain of remaining leg, which would have necessitated amputation. Graft completely relieved pain and restored leg to normal. 5 mths. after operation graft re-thrombosed, symptoms returned, and in spite of attempt to restore patency of graft lost right leg. 3 mths. later died of sudden secondary haemorrhage due to low-grade spreading sepsis along polyvinyl tube
6 7	M 64	2.5.56	Polyvinyl sponge replacement of aortic bifurcation only	Good function of graft	1 yr. 3 mths.	Very severe multiple arteriosclerotic thromboses in main artery of both lower limbs; facing amputation. Graft done to replace stricture of right common iliac near bifurcation, in hope of improving flow to right limb. Although temporary improvement occurred, rest pain recurred and right limb had to be amputated. Now, 1 yr. 3 mths. later, still has good left femoral pulse and good left leg—i.e., graft functioning well. Has angina

Diagrammatic Representation of Operative Procedures in Series II (Table II) (Numbers refer to cases. A=before and B=after operation)



invade it and grow into its interstices and incorporate it firmly into the tissues as it does with orlon; (2) it tends to break and fracture in time if it is not made thick enough; and (3) there is a high tendency to late thrombosis with this material. These disadvantages have also been found by other workers (Martin and Gaylis, 1957).

The two cases of aortic obliteration and thrombosis in which we used polyvinyl sponge prosthesis have been unsatisfactory, although in Case 6 the graft is still functioning after 15 months. As a result of the lessons learned with these cases and some experimental work of Kinmonth, Taylor, and Lee (1955) we have come to the conclusion that plastic material is unsatisfactory for replacement in cases of arteriosclerotic thrombosis. Where a short-segment replacement of a very large vessel such as the dilated aneurysmal aorta is required, then plastic material is satisfactory, and we have found that orlon tubes fulfil all the requirements here and have behaved well. The long-term results reported by other workers (Hufnagel, 1955; Kinmonth *et al.*, 1955) confirm that for aneurysms this material is perhaps better than any other, although from numerous other reports it would appear that where a fairly short segment of a large dilated vessel like the aneurysmal aorta has to be replaced then a number of synthetic substitutes will do equally well. "Nylon" and "dacron" have both been used for grafts with success.

Series III: "Disobliteration" or "Rebore" of an Occluded Arterial Segment by Direct Removal of the Occluding Thrombus

This type of operation involves direct incision of the occluded arterial segment and removal of the obstructing atheromatous plaque and the propagated thrombus. Recently we have been doing this operation through several small arteriotomy openings, using a special instrument to strip out the thrombus. We have come to call this operation "arterial rebore," for this is exactly what it is. When reboring large arteries such as in the series described here heparin solution (1,000 international units to 100 ml. of saline) is used to flush out the artery frequently during operation, but the patient is not given heparin systemically after the operation. Six patients have had this type of operation, and details are given in Table III. The indications for operation have been the same as in Series I—namely, severe claudication of the whole leg in four, and to avert amputation for a severely ischaemic limb in two.

There has been no mortality in this group and the operation has proved shorter and easier than grafting, and thus the patients have been very little upset. It is certainly a less arduous procedure than grafting, both for patient and surgeon. The follow-up has not been so long as in the first group. In one case the rebored segment has continued patent for over a year, and in three cases a good result has been maintained and the new pulse kept for over six months. In one case (Case 6) rethrombosis occurred after two months, but in this instance the operation was performed in an attempt to save a very precarious limb from amputation and was successful in this object. Recovery has been maintained in spite of thrombosis of the rebored segment, and the limb is at present in no danger.

General Assessment of Results in this Series

This type of operation in suitable cases has given perhaps the most encouraging results. The mortality has been nil, there have been no major complications, and the follow-up results to date have been satisfactory. With improvements in the technique of "rebore" we believe that the indications for this type of operation can be considerably extended.

General Discussion

Before an operation can be recommended with confidence for a given disease it is necessary first to inquire carefully into the natural history and prognosis of the untreated malady. One must be sure that any operation which may be recommended is definitely beneficial and not merely meddlesome. Moreover, in a disease which is not immediately lethal, to make an operation acceptable the risk must be low, the possible severe complications few, and its long-term results reasonable.

Arteriosclerosis is a general disease, and its most serious complication—namely, localized arterial thrombosis—may affect cerebral arteries, coronary arteries, or limb arteries indiscriminately. Arteriosclerotic changes occur not uncommonly in relatively young individuals, and appear increasingly common in the 40–60 age group.

Incidence of Coronary Disease and Cerebral Thrombosis

From our material it would appear that patients in the 40–60 age group with arteriosclerotic occlusion of a major artery are not particularly affected with coronary or cerebral thrombosis as well. There were 20 patients under 60 in this series. Of these, only one had coronary disease either

TABLE III.—*Series III: "Endarterectomy" or "Rebore" of Occluded Segment of Artery*

Case No.	Sex and Age	Date of Operation	Procedure	Result	Length of Follow-up	Remarks
1	M 47	18/6/56	Removal of obstructing thrombus from left common iliac artery	Full return of pulses	1 yr. 3 mths.	Suffered from "whole-leg" claudication of left leg at about 50 yds. Arteries very good; had small fibrosed occluding thrombus at origin of left common iliac which was easily removed. Perfect result has been maintained
2	M 71	25/4/57	Removal of obstructing thrombus involving common femoral artery	Return of femoral pulse (below area of operation)	5 mths.	Severe ischaemia of right leg with rest pain and cold feet; facing amputation. Result of operation dramatic: rest pain disappeared overnight, and now able to walk comfortably. Has since had a coronary thrombosis from which he has recovered
3	M 44	28/3/57	Removal of obstructing fibrous thrombus from left external iliac artery	Return of femoral pulse	6 mths.	In addition had a long femoral occlusion in same leg. Combination of two arterial obstructions caused severe claudication at 30 yds. Successful removal of higher block in external iliac artery brought much improvement, and now able to walk 200 yds. before claudicating and to do his job (as a waiter)
4	M 40	22/5/57	Removal of obstructing thrombus in right common iliac artery	Full return of pulses	4 mths.	Whole-leg claudication for 1½ yrs., getting worse. Has had complete relief of symptoms during period of follow-up
5	M 48	3/7/57	Removal of obstructing thrombus from right external iliac artery	Return of femoral pulse (below operation site)	3 mths.	Bilateral claudication, worse on right, due to bilateral thrombosis of both external iliac arteries; also segmental thrombosis of both femoral arteries. Right external iliac artery operated on to relieve worse leg, which was beginning to impede him in his work. To date a good result with palpable femoral pulse and relief of claudication has been maintained
6	M 57	29/7/57	Removal of obstructing thrombus from left external iliac artery	Return of femoral pulse	2 mths.	Left leg cold, painful, and near gangrene. Operation followed by rapid recovery of leg, but difficult because only peripheral channel open was profunda artery. Thrombus removed from whole external iliac and common femoral to promote flow into profunda. At 2 mths. great improvement of leg maintained, but no pulsation felt in femoral region

at the time of operation or during the follow-up period. All patients had a complete cardiac examination with an electrocardiogram before operation.

In the ten patients over 60 the incidence of coronary disease was higher. Two had angina at the time of operation (and are still alive and well with their angina three years and one year respectively after operation). One patient showed electrocardiographic evidence of coronary disease, and four months after operation had a coronary thrombosis, from which he has recovered. One patient had a cerebral thrombosis after successful resection of an aneurysm. Thus in the ten patients over 60 the incidence of associated coronary or cerebral occlusion was 40%.

It follows that operation on patients in the over-60 age group should be undertaken only where symptoms are more compelling—for example, severe pain in an aneurysm, or threatened loss of limb in a case of arteriosclerotic thrombosis. In spite of this, it is perhaps noteworthy also how low has been the operative mortality and morbidity in this group (one early death and one late death in ten cases)—suggesting that there is no need to withhold operation where an indication exists.

Natural History of Untreated Disease

When a thrombosis of a major artery occurs a collateral circulation carries the blood round the block back into the main artery beyond the block. If only one major artery is blocked the only symptom is limb claudication, which may be more or less severe depending on the patient's age and the site and length of the block. In patients under 60 the claudication often improves rapidly after the initial occlusion and stabilizes itself within about six months. It may remain static for several years and then slowly get worse as age increases. If, however, the patient is unfortunate enough to acquire a second localized block lower down in the same limb, then symptoms will be severe, and there may be rest pain, pallor, coldness, and threatened gangrene. This state of affairs, if untreated, usually leads to early loss of limb.

Effect of Restoring the Circulation Past the Higher of Two Arterial Blocks in the Same Limb

On purely mechanical principles it might be expected that if the higher or proximal block was eliminated and the high-pressure pulsatile flow down the main artery to the second block was restored, then there would be more pressure and driving force available to send the blood round the collaterals of the lower block. This should result in a decrease of the ischaemic symptoms in the periphery. Working on this premise, we performed our first by-pass of a femoral arterial block in the presence of a complete posterior tibial thrombosis in a man with gangrene of four toes in 1953. The result was astonishing, for the gangrenous tissue round the site where the toes had been amputated suddenly became alive: new healthy granulations appeared, the black sloughs were rapidly demarcated and thrown off, and the amputation healed in a matter of three weeks. This result has been maintained over three years and the patient is still walking about on this leg.

No fewer than 11 of the 30 operations recorded here were of this variety; that is to say, the patient had a severely ischaemic leg and was facing amputation. Aortography showed a major arterial block (in aorta or common iliac or external iliac), and in addition a further block of an artery or arteries lower down (such as the femoral or popliteal). Grafting or "rebore" of the upper of the two blocks was then undertaken to save the limb. This was successful in nine out of the 11 cases. Case 18 (Series I) is a typical example of this group, and the history and the result of operation are worth recounting in detail.

The patient, a woman of 57, perfectly healthy in every other respect, was limited to about 10 yards' (9.2 metres') walking by claudication in her right leg. She could not sleep for more than two hours or so at a stretch before she was woken up by the "rest pain" in her foot. Both her feet were always cold, and her right foot felt permanently numb. The claudication had first appeared about five years previously, but symptoms had steadily progressed and she had been a semi-invalid for a year. Loss of sleep particularly had made her very depressed. She had been advised that nothing but amputation would relieve her. On clinical examination of her pulses it was apparent that she probably had a blocked right common iliac artery. Aortography confirmed this, and showed in addition marked narrowing of the left common iliac artery. There was a long block in both superficial femoral arteries.

At operation on July 1, 1957, the aortic bifurcation and constricted common iliac arteries were resected and replaced by a homograft (see diagram of Case 18—Table I). Although no foot pulses reappeared owing to the blocked femoral arteries, the result of the operation was dramatic. Her rest pain and the numbness of her right foot disappeared overnight. Her feet became warm. She became a very enthusiastic sleeper—making up, as she said, for a year of wakeful nights. She is now a cheerful, not very old woman preparing to lead her accustomed active life again.

These cases are among the most rewarding in this type of surgery—representing salvage of a limb or limbs from amputation and complete rehabilitation of the patient.

Long-term Results

Our longest follow-up result is in Case 1 of Series I (homografts). This man still has a patent homograft in the common femoral artery—with all pulses present and complete freedom from claudication—four years and five months after operation. Case 3 of Series I had a perfect result from a graft of the left common iliac artery for three years and one month. The patient then died from hypertensive heart failure (one of the only two cases of hypertension in the series). At necropsy the graft was patent and "indistinguishable from normal artery." These two cases demonstrate that, provided the proper technique is used, perfect long-term results appear possible with homografts.

In addition to the two cases cited above, there have been three others in Series I in which a perfect result has been maintained, with full return of all pulses, for over two years. A further three cases have maintained a good result with all pulses present for over one year.

In Series II (plastic replacements) two polyvinyl grafts have remained patent for over one year, and two orlon grafts for 11 months and five months respectively.

In Series III (endarterectomy or rebore) one case has remained patent after one year and four months, and two cases after six and seven months respectively.

Follow-up results of under one year are not of much significance in direct arterial surgery, as delayed occlusion may occur any time within the first year. Our experience is that if a graft remains patent for a year the likelihood of late occlusion within the next three or four years is small. The first year after the operation is the critical time.

Indications for the Different Types of Operation

One of the most important technical lessons learned over the last five years is the superiority of the end-to-side type of arterial anastomosis in the handling of arteriosclerotic arteries of moderate and smaller size. This has improved the long-term results considerably. Late occlusion—after a period of six months or so—was the bugbear of end-to-end anastomosis in arteriosclerotic arteries. This is far less common with the end-to-side large lumen type of anastomosis.

On the basis of our more recent experience we have a gradually increasing preference for the closed technique of "endarterectomy" or "rebore," where the thrombus is "reamed" or "stripped" out of the artery with a special instrument through two or three small arteriotomy incisions. Improvements in technique are making this type of operation increasingly applicable. Its best indication at present is in the case where a short length of artery is blocked with fairly good artery at either end. Fig. 3 (Special Plate) shows the ideal case for this procedure.

If, however, the arteriosclerotic process involves the whole of the bifurcation and the common iliac arteries (as it often

does) the best long-term result is obtained with a homograft replacement of the whole of the bifurcation (if necessary up as far as the renal arteries), the two long ends of the bifurcation being brought down as low as is necessary to find good artery and anastomosed end to side. (Special Plate Fig. 1 well illustrates this principle.) Case 2 of Series I is a good example of how failure to observe this principle led to a poor result. A blocked external iliac artery was successfully resected and replaced by a graft. The patient remained symptom-free for a year, then the aortic bifurcation above the graft occluded, causing a return of symptoms. The aortic bifurcation was known to be extensively diseased at the time of the original operation, and for a permanent result the patient should have had a full bifurcation graft.

Finally, in aortic aneurysms we prefer a graft of orlon cloth. A number of such grafts tailored to all sorts of different sizes are kept in the theatre ready to hand for the occasion.

General Indications for Operation

On the basis of these results we now feel confident in recommending operation to any patient in the under-60 age group who has a major arterial occlusion and wants relief from his or her symptoms. If the lesion is a localized occlusion with reasonably good artery on either side, direct removal of the occluding thrombus from the artery—"rebore"—is a sound and safe operation. If the arterial disease is more widespread, a better long-term result will be obtained by radical resection of the whole aortic bifurcation and by-passing the diseased segments on each side with a stored homograft.

In the over-60 age group one's attitude is tempered by the increased likelihood of other arteriosclerotic lesions such as angina. However, even in these patients where a clear indication exists—such as pain and impending gangrene of a limb—the benefits of this type of surgery far outweigh the risks.

Aortic aneurysms tend to occur in the 60–80 age group, and here the indication is steadily increasing pain, which is the usual prelude to rupture.

Summary

A detailed follow-up study of 30 patients with either arteriosclerotic occlusion or aneurysm of the abdominal aorta and its major branches, who underwent direct arterial surgery during the last five years, is presented.

Three different types of direct arterial surgery have been used: (*a*) replacement with stored homograft; (*b*) replacement with plastic prosthesis; and (*c*) "endarterectomy" or "rebore" of the occluded segment.

The hospital mortality has been 7%. The delayed mortality (due directly or indirectly to the operation) has been a further 7%.

The specific indications for the use of these three types of procedure are given, based on the follow-up results reported.

The importance of performing an end-to-side large lumen type of anastomosis when using homografts for replacing or by-passing arteriosclerotic material is stressed, and the beneficial effect of dealing with the upper of two arterial blocks in the same limb is described.

On the basis of the follow-up results reported, and an analysis of these cases, general principles for recommending this type of surgery are suggested.

We would like to thank our many colleagues who have referred these cases. Also we record our grateful thanks to the many registrars and house-surgeons who have helped with these sometimes arduous operations, and the nursing staff of St. Thomas's Hospital and the Royal Waterloo Hospital, to whose care the low mortality in this series is largely due. We wish to thank Miss J. Dewe, our medical artist, for the illustrations.

ADDENDUM

Since this article was written one more polyvinyl graft has obliterated (Series II, Case 6). The patient has had slight increase of his claudication and symptoms in his left leg, but is in no immediate danger of amputation. This further strengthens the conclusions already mentioned above that polyvinyl alcohol sponge material is unsuitable for arterial grafting.

One further rebore of a common iliac artery and two further bifurcation grafts have been carried out successfully.

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GRAFT STERILIZATION

A BACTERIOLOGICAL AND HISTOLOGICAL STUDY OF THE RELATIVE MERITS OF ETHYLENE OXIDE AND β-PROPIOLACTONE AS TISSUE STERILIZING AGENTS, WITH SPECIAL REFERENCE TO ARTERIAL GRAFTS

BY

T. W. SUTHERLAND, M.D.
Senior Lecturer in Pathology

G. M. WILLIAMSON, M.D.
Lecturer in Bacteriology

K. ZINNEMANN, M.D., M.Sc.
Senior Lecturer in Bacteriology

AND

H. S. SHUCKSMITH, T.D., B.Sc., M.B., F.R.C.S.
Senior Clinical Lecturer in Surgery

From the Departments of Pathology, Bacteriology, and Surgery, School of Medicine, Leeds

[WITH SPECIAL PLATE]

In discussing a method for the preparation of freeze-dried arterial grafts Flewett *et al.* (1955) drew attention to the obvious advantages of using a sterilizing agent, which, they suggested, would render asepsis unnecessary during collection and would allow the use of post-mortem material for grafts. Previous workers have used either ethylene oxide (Hufnagel *et al.*, 1953) or β-propiolactone (LoGrippo *et al.*, 1955; Rains *et al.*, 1956; Berkin *et al.*, 1957).

Two questions arise if chemical sterilizing agents are used: (1) Can such agents effectively sterilize necropsy material intended for use as grafts? (2) Do such agents give rise to gross histological changes in the arterial wall? In this paper we compare ethylene oxide and β-propiolactone for sterilizing power and for failure to produce gross histological changes in graft material.

Methods

Bacteriological Investigations

Source of Material.—A total of 136 arterial and 289 bone grafts were collected for preservation. All the bone grafts and 54 of the arterial grafts were obtained by dissection under aseptic conditions. The remainder of the arterial grafts (82) were removed in the post-mortem room during routine necropsies.

Sterilization.—Ethylene oxide: a 1% solution (v/v) was used as previously described (Flewett *et al.*, 1955). β-Propiolactone: a liquid and relatively innocuous, although a concentrated solution may damage the skin and a mist is injurious to the eyes and respiratory tract. If it is carefully handled, and especially if dropping it on the skin is avoided, this agent is safe to use and has the added advantage that it is soon hydrolysed to the acid in aqueous solution. The procedure used, with almost unfailing success in our hands, is as follows. To the graft completely immersed in physiological saline and contained in a sterile tube of standard bore (Flewett *et al.*, 1955) is added sufficient β-propiolactone to give a final concentration of 1% (v/v). The tube is tightly stoppered with a sterile rubber bung and the contents are thoroughly mixed by tilting. The rubber bung is replaced with a sterile gauze-covered cotton-wool plug, and after incubation at 37° C. for two hours the fluid is poured off. The tube is then left inverted for about 10 minutes to allow surplus fluid to drain away from the graft. Any residual β-propiolactone either breaks down, is sublimed during the freeze-drying process, or is washed out during reconstruction, making any further attempts at elimination as described by LoGrippo *et al.* (1955) unnecessary.

Sampling.—Before sterilization a small portion of a number of the arterial grafts was taken for histology. Immediately after completion of either of the sterilization procedures outlined above the contents of each tube were sampled for sterility and for histological change. The sterility tests were carried out in nutrient broth for aerobic growth and in Robertson's meat medium for anaerobic growth, incubation extending over at least five days. The cultures in Robertson's meat medium were incubated in the normal manner for the first 24 hours (allowing recognition of the less strict anaerobes, in particular *Clostridium welchii*) and then in a McIntosh and Fildes anaerobic jar for a further five days (for isolation of *Cl. tetani*). After the graft material had been reconstituted in physiological saline containing 100 units penicillin, 100 μg. streptomycin, and 50 units heparin per ml., any fragments left unused were examined bacteriologically and histologically.

Since sterilized freeze-dried bone grafts are completely assimilated, as shown radiologically (Berkin *et al.*, 1957), only bacteriological examination of these was deemed necessary.

Histological Investigations

Material.—This consisted of 16 specimens of aorta or iliac artery prepared as freeze-dried grafts by the method of Flewett *et al.* (1955). The ages in years of the donors were respectively 8, 13, 17, 21, 23, 26, 29, 30, 31 (2), 32, 33 (2), 34, 36, and 37. Ten specimens were sterilized with ethylene oxide and six with β-propiolactone.

Technique.—Samples from vessels were fixed in formol-saline (*a*) before treatment; (*b*) after snap-freezing and freeze-drying, and reconstitution, but without chemical sterilization; (*c*) after sterilization alone; and (*d*) after sterilization, snap-freezing and freeze-drying, and reconstitution. Blocks from all but one of the samples of vessels after reconstitution and a few blocks from the other samples were cut as frozen sections. Blocks were taken from parts of the samples showing early atheroma or lipid flecking, whenever these lesions were apparent. Paraffin sections were stained with Ehrlich's haematoxylin–eosin, Verhoeff's elastic stain counterstained with Van Gieson's mixture, toluidine blue, and the periodic-acid–Schiff (P.A.S.) procedure. Frozen sections were stained with scarlet-red.

Results

Bacteriological

In all, 425 grafts have been sterilized and freeze-dried. The earlier ones (79 specimens) were sterilized with 1% ethylene oxide; of these, eight (10%) were still contaminated and five were discarded. The remaining three were successfully re-sterilized with 1% β-propiolactone when we became aware of its advantages. The later grafts (346) were all treated with 1% β-propiolactone, and four (1.1%) of these yielded some growth. All the failures in both series occurred with arterial grafts.

Table I shows that β-propiolactone is somewhat superior to ethylene oxide as a sterilizing agent. Furthermore, of all the grafts tested for sterility after use in the operating

TABLE I.—*Comparison of the Sterilization of Arterial and Bone Grafts With 1% (v/v) of Ethylene Oxide and of β-Propiolactone*

Graft	Ethylene Oxide				β-Propiolactone			
	No. Treated	No. Sterile after Treatment	No. Used and Examined Bacteriologically	No. Sterile after Use	No. Treated	No. Sterile after Treatment	No. Used and Examined Bacteriologically	No. Sterile after Use
Arterial	33	25 (76%)	3	3 (100%)	103	99 (96%)	23	23 (100%)
Bone ..	46	46 (100%)	35	34 (97%)	243	243 (100%)	113	110 (97%)

theatre, only 3% of both the ethylene-oxide-treated and of the β-propiolactone-treated bone grafts proved to be contaminated, and then merely with non-pathogenic cocci. This observation indicates that the process of freeze-drying as carried out in Leeds (Flewett *et al.*, 1955; Berkin *et al.*, 1957) is bacteriologically sound, and that the contamination observed may well have occurred in the operating theatre after the tube containing the graft was opened. The persisting sterility of arterial grafts following reconstitution and use in the operating theatre is probably due to the addition of penicillin and streptomycin to the reconstituting fluid.

Table II shows that the failure rate for sterilization of arterial grafts taken at necropsy is much lower with β-propiolactone than with ethylene oxide, although the ethylene

TABLE II.—*Comparison of Results of Sterilization of Arterial Grafts Obtained from Routine Necropsies With Those Taken Under Aseptic Conditions*

Source of Material	Sterilizing Agent	Number Treated	Number Sterile after Treatment
Post-mortem room	Ethylene oxide	15	9 (60%)
	β-Propiolactone	67	64 (91%)
Operating theatre	Ethylene oxide	18	16 (89%)
	β-Propiolactone	36	35 (97%)

oxide series is rather small. It must be pointed out, however, that wastage of some valuable arterial grafts because of persisting contamination after sterilization with ethylene oxide led us to abandon this technique as soon as we were convinced that β-propiolactone was superior. Although dissection in the operating theatre reduces the failure rate with ethylene oxide, the results barely equal those obtained for post-mortem material with β-propiolactone as a sterilizing agent.

Histological

Samples from vessels in groups *a*, *b*, and *c* were examined as controls.

(a) Microscopical Appearances Before Treatment.—There were no changes to be seen other than slight atheroma.

(b) Microscopical Appearances after Snap-freezing and Freeze-drying and Reconstitution, but Without Chemical Sterilization.—Sections were available from six specimens of aorta. The intima shows no more than slight fragmentation. The changes in the media are similar to those seen in samples after sterilization, snap-freezing and freeze-drying, and reconstitution (see under (*d*)).

(c) Microscopical Appearances After Sterilization Alone.—The first group comprised seven samples of aorta treated with ethylene oxide. One specimen also included part of one common iliac artery. Microscopic changes are slight and inconstant. The elastica seems slightly fragmented in the media of two specimens of aorta. Occasionally small ovoid spaces are present in the intima and media.

In the second group there were four samples of aorta and four samples of common iliac or femoral artery after treatment with β-propiolactone. In general, microscopical examination shows a very slight fragmentation of the medial elastica and a loss of metachromasia with toluidine blue. Occasional disrupted patches are seen in the intima. The changes are no more pronounced than in the specimens treated with ethylene oxide. One specimen of aorta was also stained with scarlet-red after frozen section, and this showed lipid in the intima without disruption.

(d) Microscopical Appearances After Sterilization, Snap-freezing and Freeze-drying, and Reconstitution.—Changes in the media were insignificant. Small oval spaces were formed in the media of the aorta as well as in the common iliac and femoral arteries. In specimens sterilized with ethylene oxide these spaces contain material staining metachromatically with toluidine blue, like mucin or acid mucopolysaccharide. Often this mucinoid material is limited to the margin of the oval spaces and is deeply staining. The mucinoid material does not stain with P.A.S. In specimens sterilized with β-propiolactone the space is devoid of mucinoid material, although the mucinoid material is present in other parts of the arterial wall. The elastic laminae were slightly fragmented and showed some crowding near the oval spaces. Most of these changes have been depicted by Hyatt *et al.* (1952).

Lipid in the intima, staining with scarlet-red, was present in eight out of 16 specimens subjected to frozen section. This finding emphasizes the frequency of early atheroma or "superficial fatty streaking" (Duguid, 1954) in specimens of aorta and large arteries from young subjects. The lipid was present in variable amount, but in six specimens it was moderately abundant (Special Plate, Figs. 1 and 2). The presence of lipid might be expected to lead to disruption of the intima during preparation of the graft. On the whole, however, disruption was slight, and in a graft from a man aged 34 a substantial infiltration of lipid was separated from the lumen by a layer of intact intima. In four specimens considerable infiltration was associated with only the slightest intimal disruption. In other specimens lipid infiltration was sometimes associated with the formation of oval spaces (Plate, Fig. 1) and, strikingly seen in a sample of a graft from a woman of 23, a crenellated intimal surface (Plate, Fig. 2). Often the lipid is distributed as if still contained in macrophages.

Discussion

Hufnagel *et al.* (1953) reported that 1% ethylene oxide sterilizes cultures of *Staphylococcus aureus, Clostridium welchii, Escherichia coli,* and *Bacillus subtilis* in culture media, of heterografts taken without aseptic precautions, and of such grafts deliberately contaminated with these organisms. Similarly, 1% β-propiolactone has been shown to kill *Staph. aureus* and members of the normal flora of the intestinal tract (Hartman *et al.*, 1951; Rains *et al.*, 1956) and a number of pathogenic fungi (Bernheim and Gale, 1952).

Of the two sterilizing agents examined, ethylene oxide is the more difficult to handle. It is volatile at room temperature, toxic, and explosive. These properties alone make it less suitable for use than β-propiolactone. Moreover, the results of this investigation show that it is less effective as a sterilizing agent for arterial grafts. The greater the degree of contamination the less effective is its action (see Table II). β-Propiolactone, on the other hand, is almost equally effective whether the grafts are obtained under aseptic conditions in the operating theatre or at necropsy.

When dealing with bone grafts no difference between the two sterilizing agents was apparent. This might be misleading, for in the collection of all bone tissue an aseptic "no-touch" technique has been employed hitherto (Berkin *et al.*, 1957).

Histological changes in the vessels, although slight, involve both intima and media. The most interesting change seems to have been the result of freeze-drying when pre-existing lipid was present in intimal plaques and streaks. Neither chemical sterilizing agent appears to have caused any significant structural changes.

The observations of DeBakey *et al.* (1954) suggest that the intima, after grafting, is lost or replaced by a layer of fibrin. The long-term fate of atheromatous changes in grafts remains to be determined, and such lipid accumulations must be studied by microscopical examination of grafts removed at necropsy from recipients. Duguid (1954) has emphasized that fatty lesions are almost constantly present in the aorta from childhood onwards, and are known to be compatible with long life. DeBakey *et al.* (1954) stressed that the elastica persists microscopically unchanged after grafting, and seems to support the graft during the period of organization in the host. Fragmentation of the medial elastica, seen in a few of our specimens of prepared grafts, seems too slight to cause any significant weakening of the arterial wall. Such fragmentation may have occurred during the preparation of the microscopical sections, as it is also present in a proportion of grafts treated chemically with or without subsequent freeze-drying and reconstitution.

Muscular arteries can be successfully grafted as elastic arteries, and therefore, if the views of DeBakey *et al.* (1954) are correct, it seems that the slender internal and external elastic laminae are sufficient to support the vessel wall.

Small oval spaces in the media have also been observed by Creech *et al.* (1954), who consider that they are probably the result of the formation of ice crystals during freeze-drying. These spaces appear too small and sparse to cause any significant weakening.

Summary

A technique for the sterilization of tissue grafts with 1% β-propiolactone is described.

A comparative study shows that β-propiolactone is superior to ethylene oxide as a sterilizing agent for artery and bone grafts; it has greater sterilizing powers and is much easier and safer to use.

Freeze-drying, but not sterilization with either agent, leads to the appearance of small spaces within the intima and media of the arterial wall. We are of the opinion that the spaces are too small and sparse to cause any significant weakening of the arterial wall.

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INVESTIGATION OF CHILDREN WITH SPEECH DEFECT, WITH PARTICULAR REFERENCE TO NASALITY*

BY

JAMES CALNAN, F.R.C.S.Ed., M.R.C.P.

First Assistant, Professorial Unit, Nuffield Department of Plastic Surgery (University of Oxford)

[WITH SPECIAL PLATE]

To discuss this subject within the limits of a short paper without appearing to be dogmatic is almost impossible, for I wish to present a scheme or method for the investigation of defective speech and proceed in logical sequence through it. This will require the acceptance as facts of certain statements which have not yet been incorporated into general surgical teaching although there is ample support for their veracity. These statements are in no way schismatic, but are the result of the newer knowledge concerning the speech mechanism.

First, the term "nasality" needs to be defined, for it is in popular use in this subject and commonly thought to be a definite word with an exact meaning. On the contrary, it is used to describe a feature of speech when the nose is pinched (complete nasal obstruction), when the speaker has a cold in the nose (partial nasal obstruction), when he has a cleft palate (nasal escape of air), or when he is from the Mid-Western States of the U.S.A. (increased nasal resonance). It is illogical that one word should be applied to diametrically opposing conditions, and so the more exact terms of "nasal escape" and "nasal resonance" must be used.

Nasal Escape During Speech

In the English language nasal escape is a feature of only the two consonants "n" and "m." It also occurs during the vowel "a," but is not a particular feature of that sound, although in some languages, such as Portuguese, nasal escape *is* a feature of vowels, especially when they occur as diphthongs.

According to the returns of the Registrar-General, in England and Wales in 1955 there were just under 665,000 live births, and in 1956 just over 699,000. Also it is known from several surveys in different countries (Fogh-Andersen, 1942; Ivy, 1952) that the incidence of congenital cleft lip and palate is around 1 in 700 live births, and that 70% of these infants will have palate clefts of one type or another. Allowing for 5% who will have died before their first birthday, this means that approximately 630 infants were born in 1955 with palate clefts, and all are potentially defective speakers. If all have been operated on at 1 year of age, 30% or more will still have excessive nasal escape during speech. To these 190 children each year can be added a lesser number who have other congenital speech defects associated with nasal escape, some who suffered from diphtheria, poliomyelitis, or encephalitis, and finally those who have their speech defect thrust on them by radical adenoidectomy. I have estimated the total at 250 children per year, but this is a very conservative guess, and the actual number is probably double this.

The causes of nasal escape can be summarized briefly as follows:

Causes of Nasal Escape During Speech

A. ANATOMICAL DEFECTS OF PARTS (Mechanics)
- *Congenital:* Cleft palate; submucous cleft; absence of part of soft palate or pillars of fauces
- *Acquired:* Trauma—surgical, gunshot wounds; disease—lues, cancer

B. DEFECTIVE MOTOR POWER (Dynamics)
- *Neurological:* Nuclear and peripheral:
  - Congenital: Nuclear hypoplasia
  - Acquired: Trauma; disease—diphtheria, poliomyelitis
  - Supranuclear: Congenital paresis; encephalitis; meningitis
  - Cortical: Gross mental deficiency; hysteria
- *Muscular:* Congenital agenesia—unilateral, bilateral; scar tissue

C. DISPROPORTION OF PALATE AND PHARYNX (Kinetics)
- Repaired cleft palate
- Congenital short palate
- Congenital large pharynx
- Adenoidectomy

There are numerous medical and moral reasons for treating patients with nasal escape and a sound economic motive for spending public money on them. The £8-a-week labourer who moves up into the £20-a-week skilled operator class pays back to the State as income-tax an additional £187 yearly. He has therefore paid for his treatment and rehabilitation within one year, and continues for the rest of his life to pay enormous interest for the privilege of attaining normal speech. That such a successful investment may occur has been seen in our department often enough to be impressive.

Diagnosis of Speech Defects

"Diagnosis before treatment" is as important in speech defects as it is in any other complaint, and an examination of the available aids to diagnosis is well worth while. We live in an age of great opportunity where diagnostic tools increase in quantity and quality almost daily, but they will not be produced for medical use unless they are demanded. Using the available diagnostic equipment, a scheme for the examination of patients is suggested as follows:

Investigation of a Speech Defect

History:
- Present complaint
- Past: "milestones," illnesses
- Family: of C.L. and P.; of congenital deformities; of neurological complaints

Examination:
- Inspection: palate, pharynx, tongue
- Palpation
- Auscultation: speech—articulation; nasal escape; resonance

Special Investigations:
- Audiograms
- Neurological
- Psychological; intelligence
- Social report; school reports
- Dental
- Lateral radiographs of palate
- Cineradiography during speech and swallowing
- Endoscopy
- Faradic stimulation of palate and pharynx
- Measurements of nasopharyngeal isthmus
- Biopsy

The greatest advances in diagnosis have been achieved with the help of radiology, the employment of which has enabled us to clear away many of the false ideas that hitherto prevented deliberate and conscious attempts to reconstruct our ideas concerning the physiology of the palato-pharyngeal mechanism. Roentgen announced his discovery of *x* rays in 1895 and indicated their value in medicine. Between 1895 and 1935 a total of 98 papers had been written on their use for the study of the speech mechanism, but it is only in the last few years that it has been possible to use *x* rays in the routine examination of our patients. One can indeed make a fairly complete palato-pharyngeal analysis on a simple lateral radiograph (Calnan, 1956) or, if even more accurate information is required, on a cephalometric tracing (Ricketts, 1954).

*A paper read at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, July 18, 1957.

Palato-pharyngeal Analysis

1. Soft palate: (1) length; (2) thickness; (3) site of levator eminence; (4) mobility; (5) position at rest.

2. Hard palate: (1) length; (2) relationship to arch of atlas.

3. Nasopharynx: (1) antero-posterior diameter; (2) lateral diameter; (3) movements.

4. Adenoids: size, extent, importance.

5. Tongue: control.

6. Eustachian cushions: (1) relationship to hard-palate level; (2) relationship to posterior pharyngeal wall.

Perhaps it might be as well now to see how this diagnostic scheme works in practice. I have tried to show that the object is to be a keen clinician but a somewhat reluctant surgeon, and would also point out that radiological aids may help to control treatment. Three patients with speech defects are described (Special Plate, Fig. 1) and the investigations compared and tabulated (Tables I, II, and III).

Case 1

William T. M. was born on November 23, 1922, with a unilateral complete cleft of the lip, gum, and palate on the right side (Group III 1). The lip cleft was repaired in infancy. His parents were averse to further operation and the palate cleft was never repaired. He got on well at school and was in the Army from 1941 to 1946, where as an N.C.O. he used to drill men on the barrack square. He is now 34, self-employed as a market gardener, married with one child. He wishes to improve his speech so that he may take an active part in local political affairs. He is no longer a child, but presents a problem occasionally seen in older children where there is quite good speech despite an unrepaired cleft palate, and one wonders whether this can be improved materially (Special Plate, Fig. 2).

TABLE I.—*Results of Conventional Investigation of Speech Defects*

	Case 1	Case 2	Case 3
Name	William T. M.	Janet M.	Marion T.
Age (years)	34	12	8
Work	Market gardener (self-employed)	Normal school	Normal school
"Milestones"	—	Normal	Normal
Speech began	About 2 years	At 1 year. Normal until aged 6, when—	At 1 year
Previous operation	C.L. and P. III I R. Lip repair at 7 days	T's and A's removed	Nil
Previous illness	Usual	Usual	Usual
Previous speech therapy	None (Drill sergeant 1939)	5 years	2½ years
Speech:			
Articulation	Normal	Normal	Incorrect
Nasal escape	Medium	Gross	Gross; almost unintelligible
Palate	Cleft; elevates well	Normal; no notch; elevates well	Shapely; no notch; immobile
Diagnosis	Cleft palate	? short palate; ? old polio	? old polio; ? lack of use of S.P.
Proposed treatment	Repair palate	Speech therapy	Speech therapy

Case 2

Janet M., a healthy girl aged 11, spoke normally until she was 6, when her tonsils and adenoids were removed. Immediately after this operation speech was so nasal as to be barely intelligible even to her mother. For the past five years she has received speech therapy once weekly with some improvement. Her articulation is correct, but all sounds are masked by gross nasal escape of air (Special Plate, Fig. 3).

Case 3

Marion T., aged 8, never spoke quite normally. She passed the developmental milestones at the normal times, but from the age of 3 her parents noted nasal escape in her speech, with articulatory faults which have improved only a little following 2½ years' speech therapy. She went to a normal school at 5 years and has become less shy. She is said to be in the right school class for her age and more methodical than her older sister (Special Plate, Fig. 4).

From Table I, the conventional method of investigation, it can be seen that in two cases the diagnosis is unsatisfactorily vague. In Table II further information has clarified the diagnoses, and to some extent indicated the appropriate line of treatment (Table III).

TABLE II.—*Additional Information*

	Case 1	Case 2	Case 3
Name	William T. M.	Janet M.	Marion T.
Age (years)	34	12	8
School	Got on well	Doing well	Normal standard
Social	Well adjusted	Sociable	Shy
Hearing	Normal	Normal	Normal
Dental	Arches reasonable. Instanding 43	Normal arches	Normal arches; high palatal vault
Neurological	Nil	Poker face	Nil
I.Q.	Average	103	Average
Reading age	Normal	12.1 years	Normal
Pyschological	—	Anxiety—hospitalization (Friends and mother primitive)	Anxiety
Lateral radiographs: Rest: S.P.	Reasonable length	Long and fleshy	Long and thin
Pharynx	Deep	Deep	Normal
Saying "ee"			
Blowing			
Cineradiography	Confirms incompetence	Confirms	Confirms immobility
Faradic stimulation	—	—	S.P. no reaction; pharynx brisk response
Biopsy	—	—	Scanty degenerate muscle fibres
Moulds of Isthmus	35 mm. 59 mm.	31 mm. 19 mm.	35 mm. 19 mm.
Diagnosis	Cleft palate, deep pharynx	Deep pharynx following adenoidectomy	Congenital absence of levator palati muscle

TABLE III.—*Diagnosis, Prognosis, and Treatment*

	Case 1	Case 2	Case 3
Name	William T. M.	Janet M	Marion T
Age (years)	34	12	8
Diagnosis	Cleft palate; deep pharynx	Deep pharynx following adenoidectomy	Congenital absence of levator palati muscle
Operation	4 flap V-Y palate repair	Hynes (1950) pharyngoplasty	Passavant (1879) pharyngoplasty
Moulds	28 mm. 24 mm.	31 mm. 19 mm. → 17 mm. 7 mm.	35 mm. 19 mm. → No. 10 catheter
Lateral radiographs			
Prognosis	Some improvement	Excellent	Fair
Speech therapy	No	No	Yes
Result	No change in speech		Less nasal escape; better projection of voice
Second operation	Hynes (1950) pharyngoplasty		
Moulds	13 mm. 10 mm.		
Lateral radiographs			
Prognosis	Excellent		
Speech therapy	No		
Final result	Normal speech, pitch raised	Normal speech	

Discussion

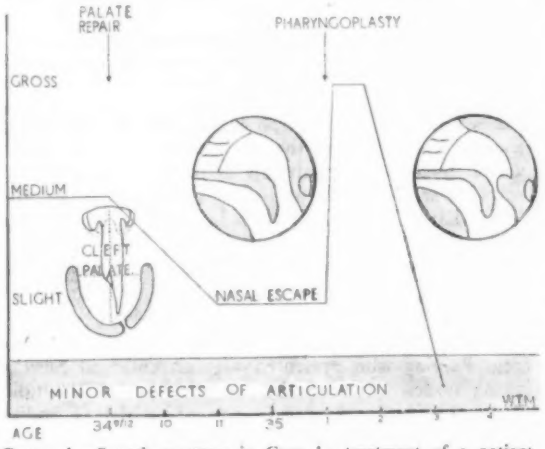
The whole object of treatment is to provide the patient with normal speech. In some cases this is impossible, and improvement is all that can be attained (Case 3). In others a surgical operation may so eliminate nasal escape that the speech therapist can complete treatment by eradicating old faults and training the patient in the correct use of the lips, tongue, and teeth during articulation. The most favourable cases to treat are naturally those with normal articulation, for in them the correct surgical treatment produces a dramatic result (Cases 1 and 2).

One could dilate further on what is normal speech and discuss the classification of defective speech. Reduced to the simplest terms, our patients may have defects of articula-

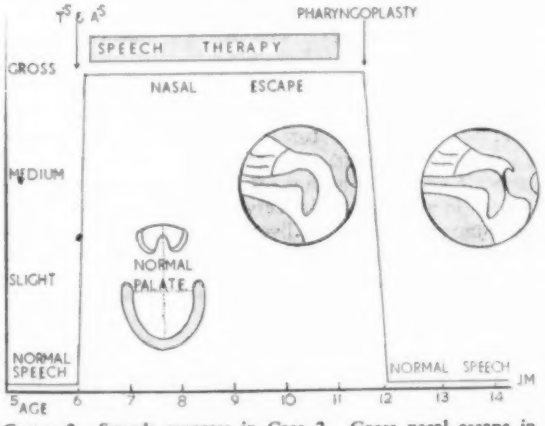
tion, of nasal resonance, or of nasal escape. This paper is concerned only with the last defect. There is, however, a fair amount of evidence to indicate that if nasal escape is reduced or, better still, eliminated, then the correction of the other two faults becomes a speedier and easier task. The reverse, the correction of articulatory faults before dealing with nasal escape, is common practice in many parts of this country and abroad; that it may be desperately hard work many patients will acknowledge.

Perhaps to understand more fully what has happened in these three patients the progress of each individual may be plotted as a graph. This form of recapitulation often points out salutary lessons for the various medical advisers. I say medical advisers in the plural, because it has been our experience at Oxford that every patient has been seen by one or two general practitioners and speech therapists, a paediatrician, an otolaryngologist, and a plastic surgeon before the diagnosis has been settled.

In Case 1 there were minor articulatory faults ("th"="f," "v"="w") which are common enough in normal speakers and so did not justify a course of speech therapy at his age (Graph 1). He has done well in life, despite his cleft, mainly because he has learnt to control the amount of nasal escape during speech. The radiographs (Special Plate, Fig. 2) suggest that the latter has been accomplished by keeping his tongue low in the mouth, thus not deflecting air up into his nose and, at the same time, making the mouth a larger resonating cavity than the nose.



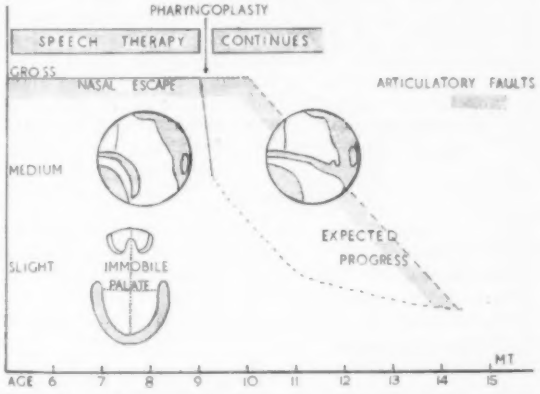
GRAPH 1.—Speech progress in Case 1: treatment of a patient with nasal escape in speech in relation to time. The amount of nasal escape fell from "medium" to "slight" after repair of palate cleft. The increase in nasal escape immediately after pharyngoplasty was probably due to oedema, limiting movement of the parts.



GRAPH 2.—Speech progress in Case 2. Gross nasal escape in speech started immediately after adenoidectomy. Five years' speech therapy did not produce improvement. Normal speech returned within a few weeks of the pharyngoplasty operation.

The patient in Case 2, on the other hand (Graph 2), was given speech lessons at weekly intervals for five years, although her articulation was correct and could not be improved further. From the radiographs (Special Plate, Fig. 3) it is equally obvious that speech therapy could never eradicate the nasal escape, and only reimplantation of the adenoid pad or some substitute could restore normal speech.

Case 3 is quite a different problem (Graph 3). Here articulation is markedly abnormal and nasal escape gross,



GRAPH 3.—Speech progress in Case 3. Gross nasal escape with gross faults in articulation had been present from the beginnings of speech. A pharyngoplasty, reducing the size of the nasopharyngeal isthmus, has already reduced the amount of nasal escape. By increasing the intraoral pressure, articulation will probably improve, but it is likely to take many years of patient speech therapy.

giving the patient unintelligible speech. In spite of 2½ years' speech therapy little progress has been made. Unfortunately, because the soft palate is immobile it is technically not possible to eradicate the nasal escape during speech without producing nasopharyngeal stenosis. One can only expect to reduce it, thereby increasing the intraoral pressure of air, which should allow the patient to take greater advantage of the help provided by the speech therapist.

These last two patients illustrate conditions which are not generally recognized but which are by no means rare. Cases similar to Case 2 are relatively easy to treat and the prognosis is good, but what the final result of treatment in cases like Case 3 will be is still unknown.

Case 2 illustrates what, to my mind, is the common clinical picture when permanent nasal escape occurs after adenoidectomy. Removal of the adenoids is the cause of the nasal escape; it is doubtful whether tonsillectomy alone ever gives rise to trouble. Unfortunately both operations are so often combined as "T's and A's," and only in special cases is either performed alone. Nasal speech immediately after operation is probably due to oedema tracking up the faucial pillars (after tonsillectomy), thereby restricting the mobility of the soft palate. Oedema is usually dissipated within three weeks, and so nasal escape must be due to some other factor—that is, loss of tissue (the adenoids) in the nasopharyngeal isthmus. This establishes disproportion between the soft palate and pharynx. Minor degrees can be overcome by greater elevation of the soft palate, so that nasal escape may be manifest only when the patient is tired, as at the end of the day; a major disproportion causes permanent and often gross nasal escape during speech, as in Case 2. The *x*-ray findings in Special Plate Fig. 3 are very typical: the soft palate, of normal length, has elevated to well above the level of the hard palate (on saying "ee . . . "), but is unable to meet the posterior wall of the pharynx, which is just too far away for contact. In a discussion on nasal speech after tonsillectomy in the *British Medical*

Journal (1956) various cures were proposed, but disappointingly little was mentioned about diagnosis. In our patient much time was wasted in conservative treatments of such kind: the logical and obvious cure is shown in Special Plate Fig. 3 and Graph 2.

In these cases one began by knowing little and believing much, and ended by inverting the quantities. The adenoids, long ago entered in the Gilbertian classification of things "that never will be missed," deserve some respect, if not a reappraisal, of their worth.

Finally, I would like to emphasize the advantages of early diagnosis and treatment in patients with speech disorders. These patients are invariably backward in reading and in their general education because of their speech defect. Some of them are of below-average intelligence and so require special help. Correcting the speech defect allows their education to proceed normally, and will also allow them to take advantage of extra coaching at school so that they may ultimately earn a living, as normal citizens, within their capacity for work and responsibility.

Summary

It is conservatively estimated that in England and Wales 250 children per year are born with potential speech defects or acquire such defects as the result of disease or of radical adenoidectomy. The mechanism of production of such defects by tonsil and adenoid operations is described.

A scheme for the investigation of children with defective speech is outlined, with particular reference to nasality. "Nasal escape" is defined and a summary of its causes given. The advantages of early diagnosis and treatment are stressed. A fairly complete palato-pharyngeal analysis can be made on a simple lateral radiograph; even more accurate information can be obtained with a cephalometric tracing.

Children with speech disorders are invariably educationally backward, and correction of the defect allows their education to proceed normally so that ultimately they may earn their living as normal citizens.

Three illustrative cases are reported. These are discussed and their progress is charted.

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Lecturing at the Royal Institution on March 21, Professor C. D. DARLINGTON, F.R.S., said that man was already controlling his own evolution, as Francis Galton had predicted he would. The present methods of control operated at several levels. Irradiation induced mutations; cousin-marriage exposed them. Selective migration and education changed our breeding groups. The successes of medical treatment increased the proportion of individuals requiring medical treatment for birth or survival. These successes also favoured a differential fertility between social classes which tended to lower the proportion of educable individuals in the next generation. Artificial insemination and medical sterilization might be used to work in the opposite direction. On a higher level we could see that the development of class structure, and the rise and decline of nations which were connected with it, were genetic and evolutionary processes. These processes were influenced or controlled to-day by the action of departments of governments, especially in health, education, and taxation. We easily forgot that, though governments could provide us with education, only parents could endow us with the ability to profit by it.

LOCALIZED LEISHMANIASIS OF LYMPH NODES

REPORT OF FOUR CASES

BY

D. W. BELL, M.B., B.S., D.T.M.&H.
Lieutenant-Colonel, R.A.M.C.

Royal Army Medical College, Millbank

J. A. G. CARMICHAEL, M.R.C.P.
Lieutenant-Colonel, R.A.M.C.

R. S. WILLIAMS, M.B., M.R.C.P.
Captain, R.A.M.C.

Queen Alexandra Military Hospital, Millbank

R. L. HOLMAN, M.B., Ch.B.
Captain, R.A.M.C.

AND

P. D. STEWART, M.D., D.T.M.&H.
Lieutenant-Colonel, R.A.M.C.

Eastern Command Laboratory

[WITH SPECIAL PLATE]

It is well known that lymph nodes may be affected in cases of kala-azar and that Leishman–Donovan (L.D.) bodies may be demonstrated in material obtained by lymph-node aspiration or biopsy (Cochran, 1912; Hu, 1936; Kirk and Sati, 1940; Lipscomb and Gibson, 1944; Rigg, 1957), but few records are available of human cases with lymph-node enlargement alone, and in which no other clinical manifestations of the infection could be found.

Chung (1944) described the case of a male student from Peiping who presented with an enlarged cervical lymph node. Microscopical examination of the node obtained by biopsy revealed the presence of L.D. bodies. Subsequent inoculation of a hamster with material obtained from an epitrochlear node gave rise to generalized leishmaniasis in the animal. The patient showed no other evidence of visceral disease over a period of four years' observation, at the end of which time he received a course of treatment ("neostibosan"—diethylamine-*p*-aminophenyl stibinate) following the development of a positive complement-fixation reaction.

Angevine *et al.* (1945) described two cases in U.S. Servicemen from the Mediterranean area who were admitted to hospital for investigation of lymph-node enlargement unassociated with any other abnormal physical signs. In both cases L.D. bodies were demonstrated in sections of the cervical lymph nodes, and, as in Chung's case, in the liver and spleen of a hamster which was inoculated with a culture made from a subsequent lymph-node biopsy from one of the cases. No other relevant case reports have been found in the literature.

Four cases are now described of British Servicemen serving in Malta and Cyprus in whom the only clinical abnormality has been the presence of enlarged lymph nodes and in three of whom L.D. bodies have been demonstrated in material obtained by lymph-node biopsy or aspiration.

Case 1

A 19-year-old soldier arrived in Malta on August 14, 1956. He trained in various parts of the island before leaving for Cyprus at the end of November. In late October he first noticed enlarged "glands" in his neck, and over the next few weeks further enlarged lymph nodes appeared in both axillae and groins. These ached and were tender to touch, but otherwise he was well. He was admitted to hospital in Cyprus, and after a right cervical lymph-node biopsy on January 2, 1957 (first biopsy), he was invalided to the United Kingdom with a histological diagnosis of sarcoid. On admission to the Queen Alexandra Military Hospital on January 29 he looked well and was afebrile. Discrete rubbery lymph nodes were palpable in cervical, axillary, and inguinal regions. There was no splenomegaly or hepatomegaly.

Investigations

Hb 15.7 g. per 100 ml.; W.B.C. 7,000 per c.mm., with a normal differential count. E.S.R. 2 mm. in one hour (Wintrobe). Serum protein 6.8 g. per 100 ml., with a normal electrophoretic pattern and a negative formol-gel test. Chest radiograph and sternal marrow normal. Mantoux reaction positive (1/1,000 O.T.). Wassermann reaction, Paul–Bunnell test, *Brucella* agglutination reactions, brucellin skin test, and dye test and complement-fixation test for toxoplasmosis were all negative.

Aspiration of a right cervical lymph node on February 20 failed to demonstrate any parasites either in direct smears or after inoculation of Novy, MacNeal, and Nicolle's (N.N.N.) medium. A further lymph-node biopsy from the left cervical region was carried out on March 1 (second biopsy).

Pathology

First Biopsy.—A lymph node 1 cm. in its greatest diameter. Microscopically, the normal architecture of the lymph node is partially replaced by discrete, clearly defined collections of large macrophage or "endothelioid" cells with a weakly eosinophilic cytoplasm (Special Plate, Fig. 1). Only occasional lymphoid follicles are present, and these show little reactive change. The sinuses are dilated in parts and contain numerous macrophages and occasional lymphocytes. The larger collections of macrophages appear towards the periphery and extend to a thickened capsule. The periadenoid tissue and capsule are infiltrated by numerous plasma cells, lymphocytes, and foreign-body-type giant cells; "tubercle"-like aggregations of macrophages are also present (Special Plate, Fig. 2). No parasites could be identified in this material.

Second Biopsy.—A lymph node measuring 2.5 × 1.5 × 1.0 cm. The cut surface has a fleshy consistency. Microscopically, the appearances are broadly similar to those of the first lymph node, but the clumps of macrophages are larger and run together to form extensive sheets of cells. Signs of early necrosis are present at the centre of some of these macrophage clumps. Multinucleated giant cells of foreign-body and Langhans types are present throughout the lymph node. The pulp is oedematous and the medullary sinuses are dilated. Intracellular parasites morphologically identical with L.D. bodies are present in macrophages and giant cells, particularly in the periphery of the lymph node. Their distribution is very irregular and a careful search is required to identify them. Smears and culture from one-half of the lymph node on N.N.N. medium failed to demonstrate any parasites.

Progress

"Pentostam" (sodium stibogluconate), 6 ml. intramuscularly daily for 10 days, was given, and one month after completion of treatment all the nodes were smaller and firmer.

Case 2

A 19-year-old soldier arrived in Malta on August 20, 1956. After about two months he noticed enlarged "glands" in the right side of his neck, but as he felt well and they were not painful he did not report sick. Soon after his arrival in Cyprus in late November the "glands" increased in size and he was admitted to hospital. On examination he was found to have enlarged, discrete rubbery lymph nodes in the cervical, axillary, and inguinal regions. The spleen was noted as "just palpable." Two lymph-node biopsies were performed, the first on January 11, 1957 (first biopsy), and the second on January 17 (second biopsy). He was invalided to the United Kingdom as a case of "generalized reticulosis." On admission to the Queen Alexandra Military Hospital on January 29 he looked well and was afebrile; the spleen was not palpable, the liver was not enlarged, and there appeared to be no change in the size and consistency of the lymph nodes as compared with their previous description. The biopsy scars were markedly indurated.

Investigations

Hb 13.1 g. per 100 ml.; W.B.C. 8,000 per c.mm., with a normal differential count. E.S.R. 2 mm. in one hour (Wintrobe). Serum protein 6.5 g. per 100 ml., with a normal electrophoretic pattern and a negative formol-gel test. Mantoux reaction positive (1/1,000 O.T.). Wassermann reaction, Paul–Bunnell test, *Brucella* agglutination, and complement-fixation and dye tests for toxoplasmosis—all negative. Sternal marrow normal. Lymph-node puncture was carried out on February 19, and the smears showed many macrophages and lymphocytes. Numerous L.D. bodies were present in macrophages (Special Plate, Fig. 3). Fluid aspirated from the lymph node was inoculated on to N.N.N. medium, but no growth took place.

Pathology

First Biopsy.—A collection of small lymph nodes, the largest being 1.0 × 0.5 × 0.5 cm. Cut section is firm. Microscopically, the lymph node shows a normal follicular pattern. Small congeries of macrophages with occasional multinucleated giant cells are scattered throughout the parenchyma, some being present in the sinuses and others in the outer zone of follicles. The peripheral and medullary sinuses show moderate dilatation and contain mainly lymphocytes and macrophages. There is no capsular thickening or periadenoid reaction. L.D. bodies are present in small numbers, both in giant cells and macrophages.

Second Biopsy.—A lymph node 1.5 cm. in its greatest diameter. Microscopically, the lymphoid follicles show marked reactive hyperplasia and there is proliferation of reticulum cells in the pulp. Clumps of macrophages, which are larger and more numerous than in the first biopsy, and giant cells are present. L.D. bodies are present within the macrophages.

Progress

After a course of pentostam there was a marked reduction in size of the lymph nodes.

Case 3

A 21-year-old soldier arrived in Malta on August 20, 1956, and trained in most areas of the island. Two months later he noticed a lump in his right groin which gradually increased in size. Unlike the other patients, he was admitted to hospital while still in Malta. On examination he was found to have enlarged femoral lymph nodes. There was no evidence of a primary focus of infection in legs or perineum. There was no other lymphadenopathy; he looked well and was afebrile. Results of investigation at that time, including white cell count, E.S.R., and chest radiography, were all normal. Two femoral lymph nodes were removed on November 28, 1956, and subsequently a histological diagnosis of sarcoid was made and the patient invalided to the United Kingdom for further investigation. The biopsy wound was slow to heal, and on the patient's admission to the Queen Alexandra Military Hospital on January 24, 1957, there was still considerable surrounding

induration. Apart from this, physical examination was negative and there were no symptoms.

Investigations

Hb 15.0 g. per 100 ml.; W.B.C., 7,000 per c.mm., with a normal differential count. E.S.R. 2 mm. in one hour (Wintrobe). Serum protein 7.9 g. per 100 ml., with a normal electrophoretic pattern and a negative formol-gel test. Mantoux reaction positive (1/1,000 O.T.). Sternal marrow normal. Wassermann reaction, Paul–Bunnell test, *Brucella* agglutination, and complement-fixation and dye tests for toxoplasmosis—all negative.

Pathology

Two lymph nodes each approximately 1.5 cm. in their greatest diameter. Microscopically, the normal architecture is widely replaced by ill-defined clumps and cords of large macrophages, amongst which are scattered numerous multinucleated giant cells of foreign-body and Langhans types. Occasional isolated giant cells are present in the pulp and lymph follicles (Special Plate, Fig. 4). L.D. bodies are present in moderate numbers in giant cells and macrophages (Plate, Fig. 5); these are more numerous in the periphery of the node and show an irregular distribution. The medullary and peripheral sinuses are dilated and the capsule is thickened and densely infiltrated by plasma cells and lymphocytes.

Progress

The patient was treated with pentostam and has remained well.

Case 4

A 19-year-old soldier arrived in Malta on August 14, 1956. Two months later he noticed enlarged "glands" in his neck, but at no time did he have any constitutional upset. He went to Cyprus in late November, where he was admitted to hospital and a left cervical lymph-node biopsy performed (first biopsy). A diagnosis of sarcoidosis was made and he was invalided to the United Kingdom. When admitted to the Queen Alexandra Military Hospital in early January, 1957, he looked well and was afebrile. He was found to have enlarged lymph nodes in the right cervical and submental regions and in the left axilla, and there was marked induration surrounding the biopsy scar. There were no other abnormal findings.

Investigations

Hb 15.0 g. per 100 ml.: W.B.C., 9,000 per c.mm., with a normal differential count. E.S.R. 2 mm. in one hour (Wintrobe). Serum protein 6.7 g. per 100 ml., with a normal electrophoretic pattern and a negative formol-gel test. Wassermann reaction, *Brucella* agglutination, Paul–Bunnell test, and complement-fixation and dye tests for toxoplasmosis—all negative. Mantoux reaction negative (1/1,000 O.T.). Sternal marrow normal. Biopsy of a left axillary lymph node was performed on March 1, 1957 (second biopsy).

Pathology

First Biopsy.—A soft lymph node 2 × 1 × 1 cm. Microscopically, the normal lymph-node architecture is completely replaced by poorly defined clumps and sheets of macrophages. Multinucleated giant cells are infrequent and occur near the lymph-node capsule, which is thickened and infiltrated by lymphocytes, plasma cells, and macrophages. The periadenoid tissue shows marked involvement in the granulomatous process, and in addition there are several foci of fibrinoid degeneration, many of which are in the walls of vessels. Eosinophilic material is also present in the centre of macrophage clumps. Despite a careful search of many sections, no L.D. bodies were found.

Second Biopsy.—Three small lymph nodes. Microscopically, all three nodes show a similar pattern. The general architecture is normal. Reactive hyperplasia and sinus catarrh are present, and two or three small congeries of macrophages with an occasional giant cell lie in the pulp. No parasites are present. Direct smears and culture on N.N.N. medium from these lymph nodes failed to show any leishmania.

Progress

Following the patient's admission to hospital in England the induration in the scar and the lymph-node enlargement gradually subsided, and after a course of pentostam the nodes became even smaller and firmer. He has remained well.

Discussion

Agius-Ferrante (1955, 1957), discussing the incidence of leishmaniasis in Malta, states that the visceral form in adults is rare on the island, and that between 1947 and 1954 only 10 cases out of a total of 777 occurred in patients over 10 years of age. He further states that there has been a significant decline in incidence of the disease on the island in the last few years, only 14 cases being notified in 1956 as compared with 204 in 1948. He makes a third observation, that the cutaneous form of the disease is never seen on the island. Debono (1957) says that, while leishmaniasis in adults does occur in Malta, it is exceptional. It is of interest, therefore, that the infection should have occurred in these four adults, within two months of their arrival in Malta, in a year in which the low incidence of the disease among the indigenous population suggests a satisfactory reduction in the number of vectors on the island. The patients were drawn from two units only, but there was no intimate contact between the personnel of these two units, and camp sites were not adjacent. In spite of repeated clinical examination over a fairly long period of observation, no further evidence of leishmaniasis was found; and, although in Case 2 it was noted in Cyprus that the spleen was "just palpable," it has not been felt on any subsequent occasion, whereas the natural history of the disease would lead one to expect a progressive enlargement if there had been a true leishmanial infection of this organ. The induration of the biopsy scars in Cases 2, 3, and 4 was a noticeable feature, and this is in accordance with the histological evidence of capsular and periadenoid infiltration.

Following a course of intramuscular injections of pentostam there was a measurable reduction in the size of the lymph nodes in Cases 1, 2, and 4, but this could not be observed in Case 3, as the only group of enlarged lymph nodes had already been surgically removed. Case 4 has been included, as there were the same movements in timing, geography, and duration as Case 1, the case presented a parallel clinical picture and showed definite clinical response to treatment, with reduction in size of the lymph nodes, and the histological picture was similar to that of the other cases. It was this basic similarity of the histological appearances of the lymph-node biopsies that first made us consider the possibility of a common aetiology. The main features are aggregations of macrophages associated with a varying number of giant cells, and in two cases severe involvement of the capsule and periadenoid tissue. Within this framework the picture varies from a few scattered foci of macrophages with occasional giant cells (vide Case 2, first biopsy) to almost complete replacement of the normal lymph-node structure by the granulomatous process (vide Case 4, first biopsy).

The microscopical appearance of organs involved in visceral leishmaniasis are well known, and are clearly described by Ash and Spitz (1945): "The basic pathologic changes in visceral leishmaniasis result from localization of the leishmania within the cells of the reticulo-endothelial system and consequent proliferation of these cells." Meleney (1925), reporting the histology of lymph nodes in experimentally infected hamsters, describes appearances very similar to those seen in our cases. He noted large clumps of clasmatocytes and multinucleated cells, and that parasites were often only present at the periphery of the clumps. Hu (1933), in reporting his work on experimentally infected hamsters,

FIG. 1A

FIG. 1B

FIG. 1.—Case 5, Series I. A: Pre-operative aortogram, showing widespread obliterative disease of aortic bifurcation and left common iliac artery with complete occlusion of right common iliac. B: Aortogram taken six months after operation, showing complete replacement by large homograft. The sites of the two peripheral end-to-side anastomoses are shown by arrows.

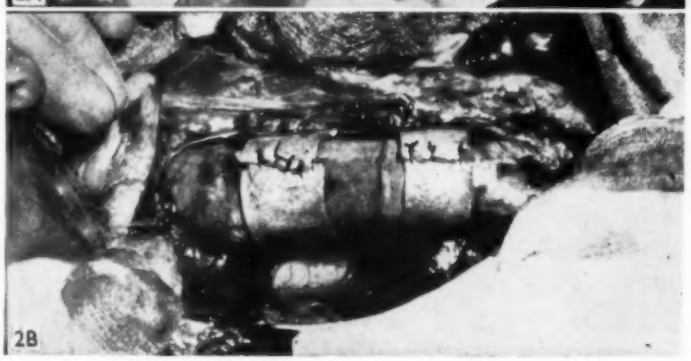


FIG. 2.—Aneurysm of abdominal aorta: (A) before and (B) after replacement by an "orlon" tube. Note method of reinforcement of anastomosis by two polyvinyl cuffs.

FIG. 3A

FIG. 3B

FIG. 3.—Case 4, Series III. A: Aortogram showing long narrowed segment of right common iliac artery. B: Operative photograph showing obstructing thrombus, which was removed from artery through two small arteriotomy incisions. (Thrombus is white object at bottom centre.)

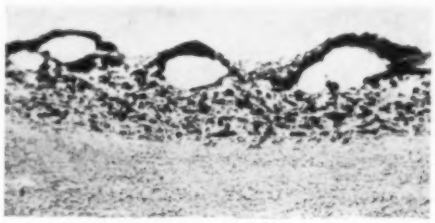


FIG. 1

FIG. 1.—Intimal lipid (black in figure) in prepared graft from donor aged 17. Lipid infiltration is here associated with formation of oval spaces. (Frozen section, stained scarlet-red. ×75.)

FIG. 2.—Intimal lipid (black in figure) in prepared graft from donor aged 23. Note crenellated intimal surface. (Frozen section, stained scarlet-red. ×20.)

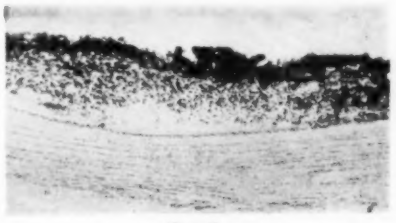


FIG. 2

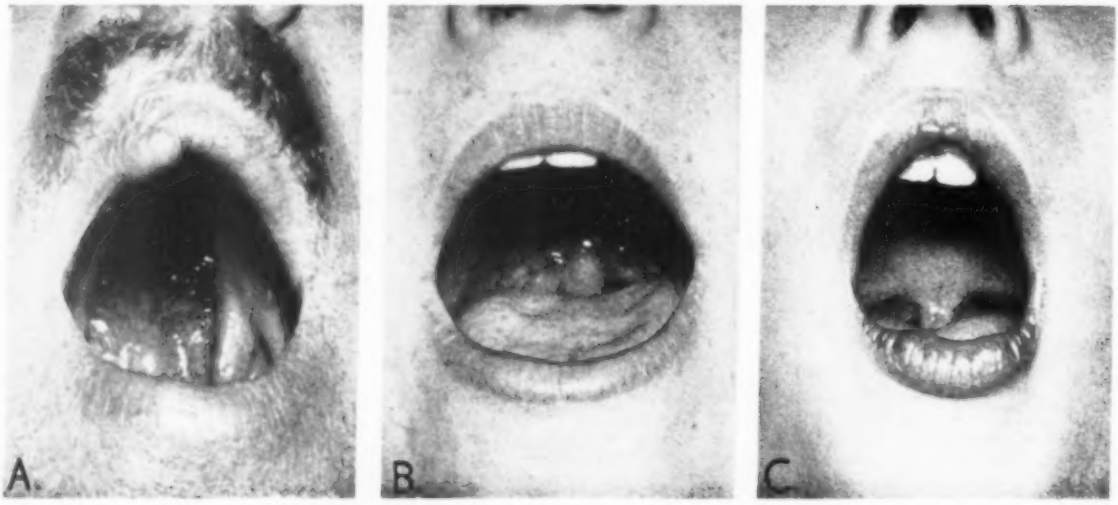


FIG. 1.—Photographs of palate in cases given as examples of speech defect. A: Wide cleft palate and deep pharynx (Case 1). B: Normal soft palate but nasal speech following adenoidectomy (Case 2). C: Normal-looking soft palate, but quite immobile (Case 3).

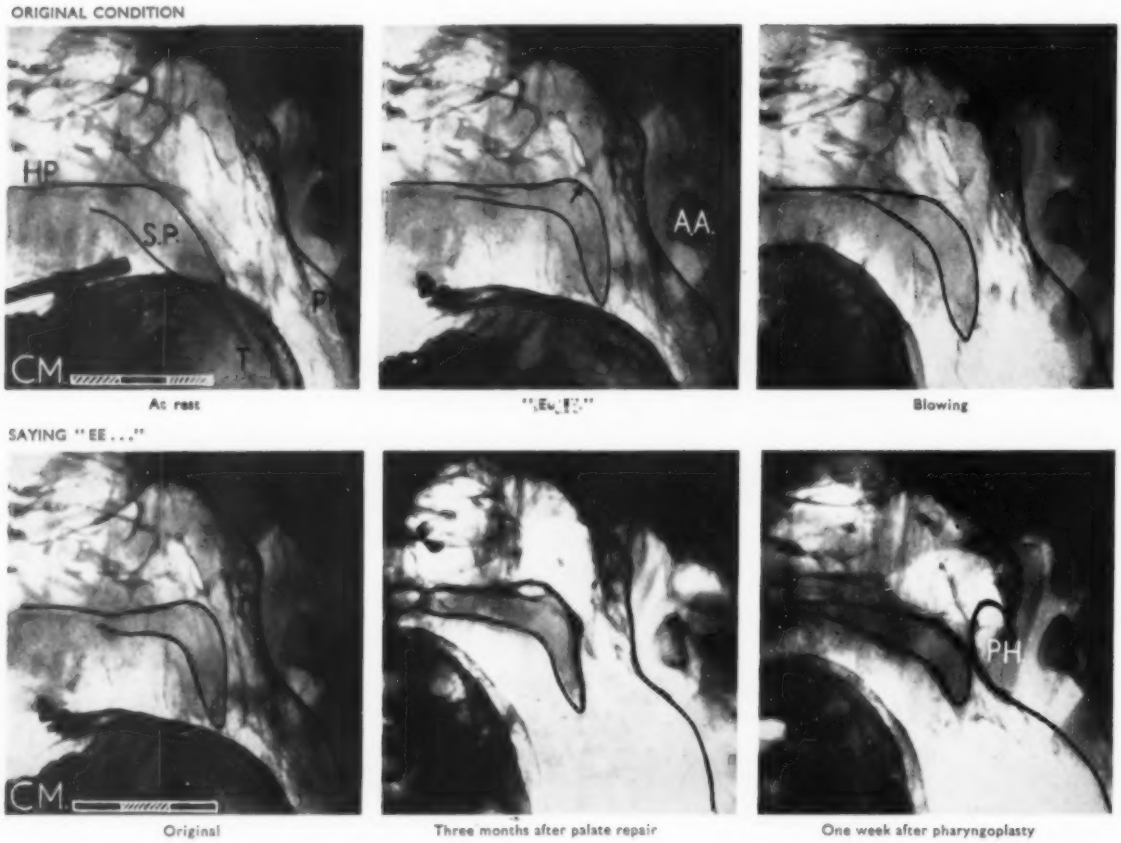
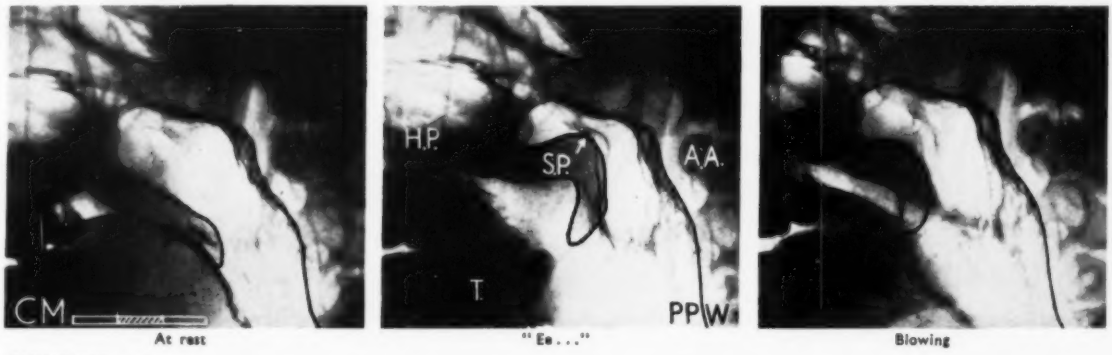


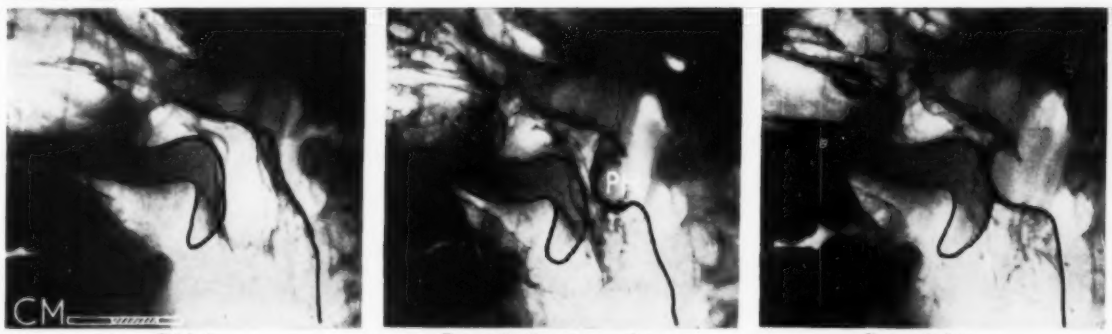
FIG. 2.—Case 1. Lateral radiographs of palato-pharyngeal region. *Above:* Original condition, when palate was cleft (as in Fig. 1A). Essential outlines have been overdrawn with indian ink for easier interpretation. H.P.=hard palate; S.P.=soft palate; T=tongue; P.P.W.=posterior pharyngeal wall. Arrow indicates site of levator eminence. A.A.=anterior tubercle of arch of atlas, an important bony landmark. *Below:* Progress towards normal speech. Soft palate has not elevated fully in last radiograph and so did not quite meet pharyngoplasty prominence (P.H.), but later did become competent.

ORIGINAL CONDITION



At rest "Ee..." Blowing

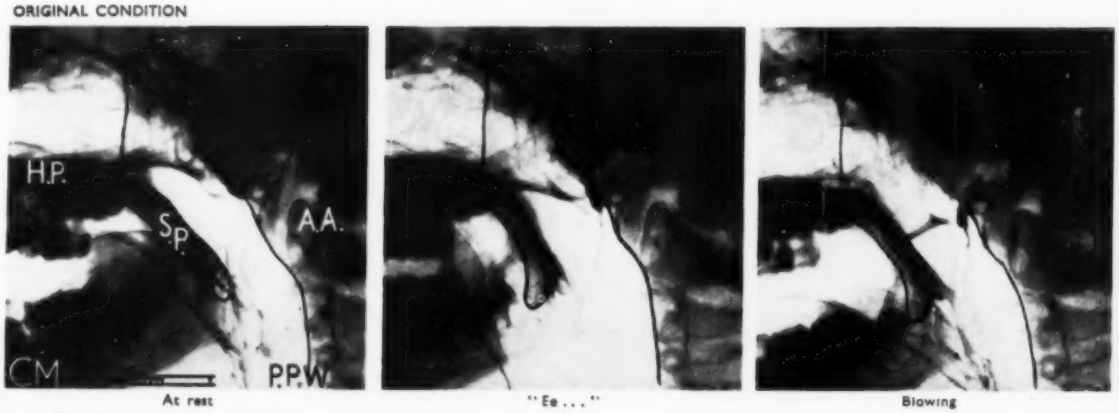
SAYING "EE..."



Original Two weeks after pharyngoplasty Six months later

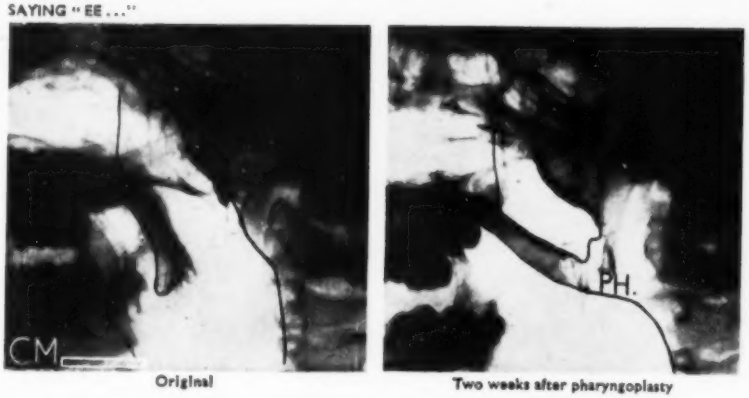
FIG. 3

ORIGINAL CONDITION



At rest "Ee..." Blowing

SAYING "EE..."



Original Two weeks after pharyngoplasty

FIG. 4.

FIG. 3.—Lateral radiographs of palato-pharyngeal region in Case 2. *Above:* One must presume that the adenoids filled the gap between the elevated soft palate and the posterior pharyngeal wall before adenoidectomy, for the patient's speech was normal. *Below:* Stages in competence of the soft palate following pharyngoplasty.

FIG. 4.—Lateral radiographs of palato-pharyngeal region in Case 3. *Above:* The soft palate, being immobile, hangs dependent when the tongue moves forward. *Below:* Pharyngeal flap pharyngoplasty has hitched the soft palate up, as well as partly occluding the oro-nasal communication.

(Landmarks in Figs. 3 and 4 as for Fig. 2)

D. W. BELL *ET AL.*: LEISHMANIASIS OF LYMPH NODES

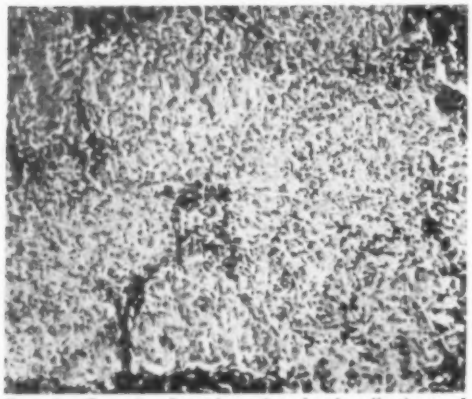


FIG. 1.—Case 1. Lymph node: focal collections of macrophages. (Haematoxylin and eosin. ×60.)

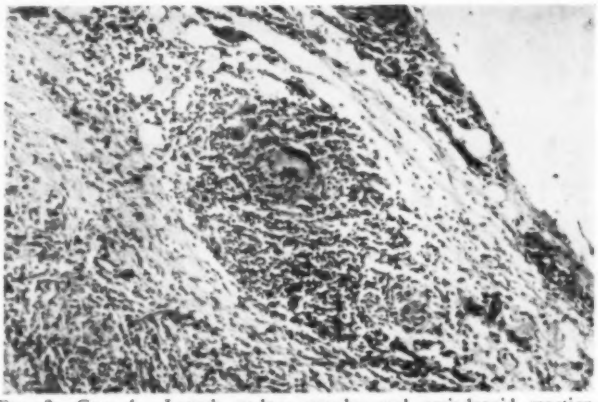


FIG. 2.—Case 1. Lymph node: capsular and periadenoid reaction. (Haematoxylin and eosin. ×60.)

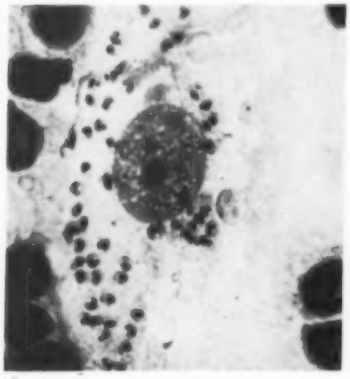


FIG. 3.—Case 2. Lymph-node puncture: L.D. bodies. (Leishman. ×750.)

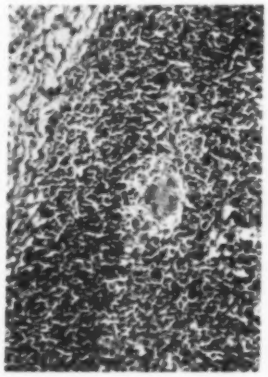


FIG. 4.—Case 3. Lymph node: giant cell in follicle. (Haematoxylin and eosin. ×60.)

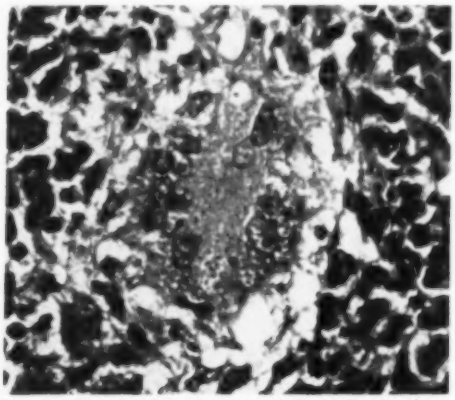


FIG. 5.—Case 3. Lymph node: L.D. bodies in giant cell. (Haematoxylin and eosin. ×480.)

R. O. K. SCHADE: EXFOLIATIVE CYTOLOGY OF GASTRIC CARCINOMA

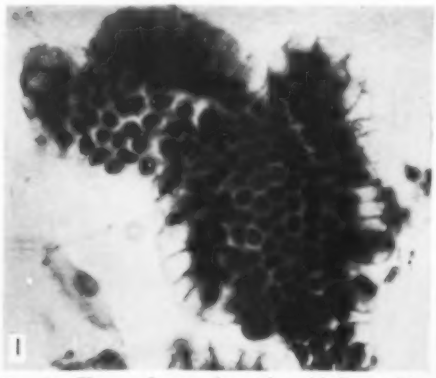
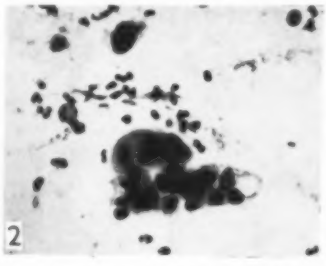


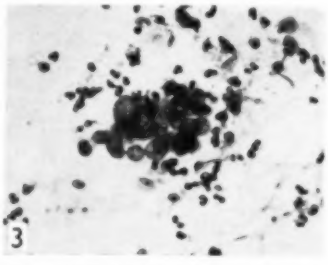
FIG. 1.—Clump of normal gastric epithelium with regular structure and nuclei of equal size. Cell boundaries are well defined. (×712.)

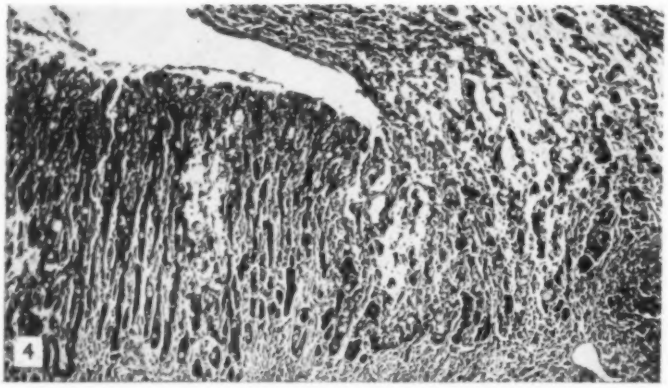
FIG. 2.—Clump of malignant cells showing overlapping and variation in size of nuclei. The background is formed by squamous cells, organisms, and polymorphs. (×475.)

FIG. 3.—Group of malignant cells denuded of cytoplasm. Note variation in size of nuclei and prominence of nucleoli. Polymorphs and organisms form the background. (×475.)

FIG. 4.—Typical mucoid carcinoma, entirely confined to the mucosa. (×165.)







described tubercle-like collections of macrophages in lymph nodes and an increase in the number of plasma cells in the medullary cords of lymph nodes. Angevine *et al.* described similar changes in the lymph nodes of their two cases.

Identification of the parasites requires a careful search of many sections. Angevine *et al.* also noted this and found parasites were more numerous at the periphery of the node. They suggest that if fixation does not reach the parasites quickly they degenerate. The difficulty of finding the parasites is well illustrated in Case 1 (second biopsy). After surgical removal the lymph node was bisected, one-half being placed in 10% formol saline for histological processing, and smears and imprints made from the other half. Parasites were identified in the paraffin sections, but none could be found in the smears.

Various staining methods were used, including Giemsa, but the most satisfactory results were obtained with routine haematoxylin and eosin. It was noted that the parasites were P.A.S.-negative. No tubercle bacilli or fungi were demonstrated in any of the lymph nodes.

Our lack of success in culturing the parasites was disappointing. One of the reasons for this failure may have been that only a very small amount of fluid was obtained by aspiration of the lymph nodes, and most of this was used in the preparation of the smears, leaving only traces in the needle for cultural purposes. Unfortunately the cultures prepared from the excised lymph nodes were contaminated.

Many disease processes involving lymph nodes, including sarcoidosis, tuberculosis, and histoplasmosis, may present similar microscopical changes to those described above, and the differential diagnosis on histological grounds may be difficult. It is a matter of interest that in three of our cases an initial diagnosis of sarcoidosis was made.

The possibility of the occurrence of this condition should be considered by both clinicians and pathologists in the differential diagnosis of lymphadenopathy in patients from areas of endemic leishmaniasis.

Summary

Four cases of leishmaniasis are described in which the disease appears to have localized to the lymph nodes. The literature on this subject is briefly reviewed.

Histologically, the lymph nodes showed a chronic granulomatous reaction, and the presence of Leishman–Donovan bodies was demonstrated in three of the cases.

Attention is drawn to the possibility of the occurrence of this condition in the differential diagnosis of lymph-node enlargement occurring in patients who have been in areas of endemic leishmaniasis.

We are indebted to Dr. I. A. B. Cathie, of the Hospital for Sick Children, Great Ormond Street, for performing the toxoplasmosis complement-fixation and dye tests, and to Mr. D. E. Tomkinson, of the Royal Army Medical College, for the photomicrographs.

ADDENDUM

Since this paper was written a further case has come to light: in a soldier aged 20 from the same unit as Cases 1 and 4. He presented with cervical lymph-node enlargement, and biopsy revealed a similar histological picture with L.D. bodies.

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EXFOLIATIVE CYTOLOGY OF GASTRIC CARCINOMA*

BY

R. O. K. SCHADE, M.R.C.S., L.R.C.P.

Senior Lecturer, Department of Pathology, Royal Victoria Infirmary, Newcastle upon Tyne

[WITH SPECIAL PLATE]

Although it is generally assumed that cytological studies of gastric material are recent in origin, the literature of the last century contains several papers which point out the importance of a histological study of gastric washings. Rosenbach in 1882 observed tumour particles in gastric washings, and Samuel Fenwick in 1895 described the presence of gastric mucosal fragments in gastric aspirations. Similar observations were made by French workers. However, these studies were not pursued until Papanicolaou's work gave us a renewed stimulus for this type of investigation.

At the request of my surgical colleagues I began the cytological examination of gastric cellular material about four years ago in an attempt to achieve earlier diagnosis of gastric carcinoma. In preparation for this task I made smears from fresh operation specimens of benign and malignant conditions of the stomach in order to obtain some idea of the cellular structures that one may find in gastric aspirations. The next step was to decide which of the many methods for obtaining cellular material should be used.

At the time two essentially different ways of obtaining cellular material were in use: (1) those methods which aimed at a mechanical removal of mucosal tissue, and (2) lavage techniques which used a fluid with or without mucolytic agents. The gastric brush and the abrasive balloon belonged to the first group; lavage with saline or Ringer's solution of a fluid containing papain or α-chymotrypsin belonged to the second.

Technique

We decided to use the least-complicated lavage method, a method advocated by the group of cytologists working in the Vincent Memorial Hospital (1950). This technique is as follows.

The patient fasts for 12 hours before the test. In the morning a Levene tube with additional openings is passed into the stomach, either through the nostril or by the mouth while the patient drinks a glass of water. The stomach is then emptied with a 50-ml. syringe. The material so obtained represents the first specimen. Then 100–200 ml. of saline or Ringer solution is injected through the tube under pressure, the fluid being partially withdrawn and reinjected several times. After clamping of the tube the patient is asked to assume varying positions to allow close contact of the fluid with as large an area of gastric mucosa as possible. The fluid is finally aspirated as completely as possible, and represents the second specimen. These specimens are sent to the laboratory immediately after they have been obtained. They are centrifuged at 2,000 r.p.m. The sediment is spread on four to six slides, fixed in alcohol-ether, and stained by Papanicolaou's method.

The smears may contain exfoliated squames from the upper digestive tract and gastric mucosal fragments as well as inflammatory cells. Aspirated sputum may be mixed with gastric material; therefore bronchial epithelium and

*Read to the Section of Surgery at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

carbon-laden phagocytes may be found. Undigested particles of food and a variety of organisms are seen according to the pathological changes in the stomach.

Normal mucosa (Special Plate, Fig. 1) is characterized by the regularity of its structure. The columnar cells that line the stomach are clearly seen. The cells are equally spaced, their cellular outlines being well defined. The nuclear chromatin shows no abnormal clumping and there is no variation in size and shape of nuclei.

In contrast to the normal epithelial cells the malignant cell groups show the following characteristics: (1) The tumour cells appear very frequently as clumps in which the nuclei are more closely approximated to each other—often there is overlapping of nuclei; (2) the nuclei show irregular chromatin structure; (3) the nucleoli within the nuclei may be large and are often present in increased numbers; (4) the nuclear membrane stains intensively; (5) the nuclei may show hyperchromasia; (6) the nucleo-cytoplasmic ratio is changed in favour of the nucleus; (7) there is a great variation in cell size; and (8) the cytoplasmic outline may be indistinct. Some of these features are seen in Figs. 2 and 3 on the Special Plate. Malignant cell groups rarely show mitoses.

Besides these cytological criteria we look for the following features in the smears, as they are often found in the presence of carcinoma—namely, large numbers of polymorphs, plasma cells, fresh, diffusely distributed erythrocytes, and an abnormal bacterial flora which is an indicator for the presence of achlorhydria.

Results

So far, about 2,500 gastric cytological examinations have been made. Twenty-five cases of carcinoma have been discovered by cytology where other investigations (radiology and gastroscopy) have been negative. Whenever an operation specimen has been received the cytological findings have been carefully correlated with the morbid anatomical changes found in the stomach, which has been opened along the lesser curvature, pinned out flat, and fixed immediately after excision. One important conclusion to be drawn from our experience is that the best material for cytology was obtained from those cases in which the malignant lesion was subsequently found to be small, often confined to the mucosa. Paradoxically, the material most difficult to interpret comes from those cases in which the tumours are large and widely ulcerated. The lavage fluid of these cases contains much debris and many organisms and inflammatory cells which make cytodiagnosis difficult or impossible.

As a result of cytological investigation we have seen a number of cases in which the tumour was as yet entirely confined to the mucosal layers and no lymph-node metastases could be found. The following are two illustrative cases.

Case 1.—A woman aged 72 had complained of dyspeptic symptoms and loss of weight for three years. A barium-meal examination in 1955 showed no abnormality. On readmission in January, 1957, her test meal showed an achlorhydria; the barium-meal report stated: "The radiological features of abnormality in this stomach are not very convincing." Gastric cytology showed undoubted malignant cells. At laparotomy no palpable tumour was found, but the wall of the pyloric antrum was oedematous. A partial gastrectomy was performed. Macroscopically, the pyloric antrum was the seat of a surface carcinoma, 7 cm. in diameter, which was covered by an inflammatory exudate. Histologically, it proved to be a typical mucoid carcinoma (Special Plate, Fig. 4) confined to the mucosa and nowhere infiltrating the muscularis. The remaining gastric mucosa showed chronic atrophic gastritis with widespread intestinal metaplasia. Large areas of the body mucosa were the seat of severe gastritic changes. No lymph-node metastases were found. Three months after the operation the patient was symptom-free and had gained 10 lb. (4.5 kg.) in weight.

Case 2.—A man aged 44, admitted in 1952, complained of stomach pain and loss of weight. The test-meal examination revealed achlorhydria; the barium-meal examination was negative. After two years he was readmitted for gastroscopy and a barium-meal examination. The former showed a small ulcer in the lesser curve, but the latter was again negative. Cytology of this case indicated the presence of malignant cells. Carcinoma was confirmed by the appearances of the operation specimen, the pyloric antrum showing chronic atrophic gastritis and a flat superficially ulcerated carcinoma (5 cm. in diameter) which infiltrated the submucosa at only one point. No lymph-node metastases were found.

These and similar cases, diagnosed by cytology, presented morbid anatomical appearances which were entirely new to us. Never before had I observed a gastric carcinoma limited to the mucosa, and only a few such cases—found accidentally at necropsy or in operation specimens—are described in the literature. It therefore appears that cytology can discover gastric carcinoma at a very early stage, even at a time when the operating surgeon may not be able to feel the lesion, as the tumour is entirely confined to the mucosa.

It is of great interest that these carcinomata arise in stomachs the mucosa of which has undergone a profound structural alteration. Some form of chronic atrophic gastritis is invariably present, often with widespread intestinal metaplasia, a condition which is regarded by some pathologists as a precancerous lesion. Our findings seem to lend some support to this conception. In addition, chronic atrophic gastritis is clinically associated with an achlorhydria, and achlorhydria is present in most cases of gastric carcinoma.

It has often been stated that chronic gastritis is a lesion which develops secondarily to carcinoma, possibly as a result of obstruction. The small carcinomata seen in our specimens do not support this assumption.

Study of the case histories of the patients with "surface carcinoma" has taught us that this type of carcinoma develops very slowly, and it may take from two to three years before the surface carcinoma develops into the carcinomatous tumour we are more familiar with.

Therefore it must be our aim to detect the tumours while they are still confined to the mucosa.

Conclusion

I would like to express the opinion that patients with an achlorhydria which is always associated with structural mucosal changes such as a diffuse chronic atrophic gastritis should be investigated until it has been proved that there is no evidence of carcinoma. Cytological examination, to which few patients object, is an easy method for screening and following up. Finally, the gastric cellular material reflects better than any other method the pathological processes of the entire gastric mucosa, and can provide satisfactory diagnostic results which compare favourably with radiological and gastroscopical findings.

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A conference on cerebral palsy was held at the Duchess of York Hospital for Babies, Manchester, on February 15 under Professor W. GAISFORD'S chairmanship. Paediatricians, orthopaedic surgeons, medical officers of health, and physiotherapists attended. In the morning papers were read, and during the afternoon session Mrs. BOBATH gave a demonstration of her methods of physiotherapy on a series of children whom she had never treated previously.

CLINICAL ASPECTS OF CARCINOMA OF STOMACH IN DIAGNOSIS

BASED UPON THE STUDY OF 146 CASES*

BY

JOHN GILMOUR, M.S., F.R.C.S.

Surgeon, Royal Victoria Infirmary, Newcastle upon Tyne

The clinical diagnosis of gastric carcinoma, with its subsequent treatment, remains one of our most challenging problems. Its magnitude may be gauged from the fact that the stomach is the commonest site of malignant disease. Fully 40% of gastro-intestinal cancers occur in the stomach. It accounts for one-third of all cancers in men and for one-fifth in women, and 15,000 persons die annually of the disease in Great Britain. Again, whilst it is true that modern surgical management has extended the range of operative treatment to over 50% of its sufferers, and has reduced the immediate mortality rate, it is still lamentably true than only about 10% survive resection for five years or over. The important point here is that these are patients in whom lymphatic spread is either absent or very strictly localized.

The trend of modern thought is therefore to consider how to establish the diagnosis at a earlier stage in the disease process. This will depend upon a better appreciation of the clinical features of early carcinoma, a greater knowledge than we at present possess of the precancerous states of the stomach, and the reliance which the radiologist, the gastroscopist, and the cytologist can inspire by the accuracy of their reports in early cases. The primary responsibility for singling out the patient with suspicious symptoms of gastric cancer remains with the family doctor, and the surgeon whom he consults should be prepared to admit the patient without delay for study and investigation.

Present Series

Gastric carcinoma is a disease of adult life. Table I shows the age and sex incidence in a series of 146 patients with gastric carcinoma dealt with in my wards at the Royal Victoria Infirmary. Of these, 70% had no previous history of ill-health, but their symptoms ranged from a few weeks to one year, with an average duration of between five and six months; 15% had dyspeptic histories of one to five years, and 15% had had stomach trouble for many more years. In the majority, therefore, we are confronted by an adult patient suffering from his stomach for the first time, but in a large minority there is a previous gastric history which requires the closest attention.

TABLE I.—*Age and Sex Incidence*

Ages	Males	Females	Total
30–39	3	2	5
40–49	16	4	20
50–59	35	15	50
60–69	34	12	46
70–79	19	4	23
80–89	—	2	2
Total	107	39	146

Youngest male, 34. Youngest female, 38. Oldest male, 79. Oldest female, 85.

The problem of gastric carcinoma is complicated because the disease may originate at any part. In my series the distribution was: pyloric segment, 44%; lesser curvature, 14.7%; body, 29.3%; cardia, 12%. Again, it occurs in several forms, and Borrmann's classification (Table II) is a useful reminder.

*Read in the Section of Surgery at the Annual Meeting of the British Medical Association, Newcastle upon Tyne, 1957.

The signs and symptoms naturally vary with the site of the growth, its extent, and its type; but there are three overriding factors which are primarily responsible for the symptoms, and the resulting clinical features of any one case are due to one or more of these factors. These are: (1) the constitutional or toxaemic effects of the growth; (2) the effects of its ulceration upon the individual; and (3) the mechanical effects of carcinomatous infiltration of the gastric musculature or obstruction of its orifices or lumen.

TABLE II.—*Pathological Types—Incidence*

1. Polypoid Tumours. Single, of low malignancy; infiltrate late; bleed readily, causing anaemia	7·5%
2. Localized Carcinomatous Ulcers. Infiltrate slowly—clearly defined edge	21·0%
Ulcer-cancers	14·6%
3. Ulcerating Infiltrating Carcinomas. Spread and disseminate quickly, advancing edge beyond ulcerated surface	23·0%
4. Diffuse Non-ulcerating Carcinomas:	
Localized form as a plaque, annular or conical growth	23·0%
Linitis plastica; leather-bottle stomach	10·8%
Spread slowly and infiltrate widely; disseminate by lymphatics late.	

Constitutional or Toxaemic Effects

The constitutional or toxaemic effects of a carcinoma are due to its metabolites and are most pronounced in cellular growths which proliferate, infiltrate, and disseminate rapidly, whilst they are less marked in the more localized carcinomatous ulcer, ulcer-cancer, and fibrotic scirrhus.

The following are most likely to attract early attention: (*a*) The *fatigue syndrome*, in which general lassitude, malaise, and mental apathy are the chief symptoms. (*b*) *Anorexia*, which is commonly present, particularly when there is hypochlorhydria or achlorhydria, and which progresses until there is repugnance for food and particularly for meat. However, in ulcer-cancers with free hydrochloric acid in the gastric juice appetite may be retained. (*c*) *Loss of weight*. This is important: it is usually gradual but persistent, though it becomes rapid when there is either pyloric or cardiac obstruction. (*d*) Development of a tendency to *constipation*. (*e*) A relatively *low blood pressure*: this is a frequent feature.

In my series there were six cases in which toxaemic symptoms predominated. These were patients with marked fatigue and loss of appetite who had large inoperable growths in the middle segment of the stomach.

Effects of Ulceration of Growth

Ulceration of the growth may result in (1) occult haemorrhage—anaemia; (2) overt haemorrhage; or (3) perforation.

1. Ulceration commonly causes a chronic loss of blood as this drips from the surface. In addition, protein, electrolytes, and fluid escape from the ulcer, and a secondary anaemia of the hypochromic microcytic type develops which will respond temporarily at least to iron treatment and blood transfusion. Pallor, dyspnoea or exertion, giddiness, and exhaustion may therefore be the primary sign of a "silent" carcinoma or may develop as a complicating condition in a dyspepsia due to carcinoma. Mention should be made of three other types of anaemia which may occur in gastric cancer. There may be hyperchromic megaloblastic anaemia —that is, Addisonian in type—when the growth has destroyed the source of the intrinsic factor, or a true pernicious anaemia in which a general atrophy of the body mucosa is associated with a carcinoma. Treatment with vitamin B_{12} will restore the blood picture in both instances. Finally, there may be a leuco-erythroblastic anaemia due to a fine widespread dissemination of cancer cells throughout the bone marrow, and this, of course, is an irreversible condition: destruction of the supply of blood platelets may result in a purpuric rash. The key to the problem of unexplained anaemia lies, therefore, in a blood examination and in the

discovery of occult blood in the stools. Of the 20 cases in which anaemia was the primary condition and ulcerating lesions or polypoid growths were responsible, 14 were resectable.

2. *Overt Bleeding.*—Haematemesis and melaena are commonly regarded as complications of acute or chronic peptic ulceration, but it is important to remember that occasionally a severe haemorrhage may come from a carcinoma. This happened in 12 cases and accelerated admission to hospital in five of them. Its earlier occurrence in patients with long histories of gastric trouble is apt to be misleading, for in such it is easy to forget that the latest haemorrhage may have a carcinomatous origin. The importance of discovering its source needs no emphasis; the same applies when the vomit has a coffee-grounds appearance.

3. *Acute perforation* of a carcinomatous ulcer is rare. It occurred in six cases; two were in early growths and both were resected. In a suspicious perforation a biopsy or immediate partial gastrectomy should be done. It is interesting to record that one of those patients is alive and well after nearly 10 years. Subacute perforation also occurs, and may result in a localized abscess. Late in the disease it may cause a septic peritonitis to be superimposed upon a carcinomatosis peritonei with ascites.

Mechanical Effects of Carcinoma

The mechanical effects of a carcinoma are due either to local muscular infiltration or to obstruction of one or other orifice or lumen. When local infiltration occurs the affected segment of the stomach wall can neither relax during gastric filling nor contract when peristalsis occurs. Dyspeptic symptoms result which may be mild to begin with, but which increase in severity and in duration as the growth extends, until pain is continuous and occurs also at night. This must be due to the increasing embarrassment caused by the growth and the greater peristaltic effort required to empty the stomach. At the same time emptying tends to be incomplete and vomiting ensues until in some cases with retention it occurs at four- to six-hourly intervals.

It is noteworthy that dyspeptic symptoms are most pronounced when the growth lies on the "gastric canal"—that is, the lesser curvature, the pyloric antrum, and canal, the area of deep peristalsis—and that symptoms are less marked when the weaker musculature of the fundus body or upper half of the greater curvature is involved.

Thus the site of infiltration is more important than the type of growth. This explains why different types of growth may produce the same symptoms and why the same type of growth may cause different symptoms in two patients.

In practice the dyspeptic symptoms of carcinoma have a distinct time relationship to the gastric cycle, and if those of obstruction are added we can recognize five primary types: filling dyspepsias, pyloric mill syndrome, gastric ulcer syndrome, duodenal ulcer syndrome, and obstructive syndromes.

Filling Dyspepsias

The filling dyspepsias are characterized by the onset of symptoms during or immediately after food, with aggravation by more food, and relief from vomiting. The first symptom is often a sense of fullness after eating. In time this becomes a discomfort, later an ache, and finally a pain. Sometimes the primary complaint is of flatulence at table with relief from belching. Occasionally there is nausea without pain. It may occur before breakfast or follow a meal. Vomiting will always relieve it.

Again, the only symptom may be a sudden attack of vomiting during or after food. This may point to an early pyloric or cardiac obstruction. As a late symptom vomiting usually follows pain. Such an attack may recur, and is apparently due to local spasm or oedema at the orifice set up by the growth. Its significance should not be overlooked, for it heralds the approach of a more complete malignant obstruction. When the growth is on the fundus or body the first symptom may be the inability to complete a full meal, or a sense of fullness after a small meal. The late picture may therefore be that of a filling dyspepsia complicated by loss of appetite and weight and some degree of anaemia.

Filling dyspepsias are relatively common in gastric cancer because they arise with growths on the lesser curve and pyloric segment of the stomach. In my series 35 patients had this syndrome, and milder dyspepsias of this type occurred in 14 out of 26 patients whose primary complaint was of anaemia or exhaustion.

Pyloric Mill Syndrome

A few patients insist that their symptoms began about a quarter of an hour after food and might last for periods of up to an hour. They had discomfort or pain aggravated by food and relieved by vomiting, which frequently occurred. Alkalis might also ease the pain. They became afraid to eat. Their complaints are therefore similar to those with filling dyspepsias but differing by the short period of freedom after a meal. Naturally if they had a filling dyspepsia instead, followed by vomiting, they could not develop a pyloric mill syndrome, which coincides with the onset of digestive gastric activity. The causal lesion lies on the lesser curvature and the pyloric antrum, but not in the pyloric canal. There were eight examples in my cases, and in one the growth lay high on the lesser curve.

This syndrome differs from that of a chronic gastric ulcer by the shorter interval of freedom from pain after food; by the fact that food immediately aggravates and does not relieve the pain; and by the greater frequency of vomiting in the early stages. On the other hand, the relief from alkalis will tend to confuse the diagnosis.

Gastric Ulcer Syndrome

In the gastric ulcer syndrome of carcinoma there is pain one to two hours after food, with relief from more food, from alkalis, and from vomiting when it occurs. These symptoms are naturally a fruitful source of confusion and delay in diagnosis. There are other difficulties. (1) The improvement obtained from bed rest and lavage in gastric ulcer may also be seen in carcinoma, when this can be attributed to the alleviation of the associated chronic gastritis. (2) Though a scirrhous carcinoma may be the cause of the symptoms, ulcer-cancers and localized carcinomatous ulcers are the commoner causes and there may be some difficulty in differentiating them from chronic ulcer. (3) In about 30% of those with ulcer symptoms the clinical history may extend over several years and simulate simple ulcer. (4) In cases of ulcer-cancer, as in simple ulcer, there is often free hydrochloric acid in the gastric juice and a good appetite is retained.

The danger lies in persevering with medical treatment too long on the assumption that the ulcer is simple. Malignancy is to be feared when the ulcer is prepyloric, or occurs on the greater curve, in any case when there is achlorhydria, when relief from food and alkalis grows less and vomiting becomes more frequent, and when the pain loses its periodicity. In ulcer-cancers the symptoms may change dramatically—the pain becomes less severe but more constant, and vomiting gives shorter relief. Appetite may suddenly disappear. Additional help is got by finding occult blood frequently in the stools or when the vomit becomes foul-smelling and has the appearance of coffee grounds. Clinically the absence of the "deep tender spot" of a chronic ulcer and the possible presence of a palpable lump are significant.

All cases with the ulcer syndrome should be admitted for investigation. If a positive diagnosis cannot be made the patient should be retained in hospital under medical treatment for two to three weeks and then reinvestigated thoroughly. In case of further doubt a surgical resection is amply justified. Opinions differ about the percentage of chronic ulcers which become malignant. In 168 resected carcinomas at the Royal Victoria Infirmary, 13.7% were

histologically proved ulcer-cancers, and in my own series the percentage was 14.6. Again, it is frequently stated that in 15% of carcinomas there is a previous history of peptic ulcer.

Of the 31 patients in my series with this syndrome only 14 were resectable—a clear indication for an earlier and more exact investigation of the group.

Duodenal Ulcer Syndrome

The duodenal ulcer syndrome of carcinoma deserves to be better known, for the pain occurs two to three hours after food, is often a true "hunger pain," and is relieved by food and by alkalis. Vomiting is infrequent. It occurs when the stomach is contracting down, and is associated with lesions on the pyloric canal and the adjacent parts of the antrum and lesser curve. These are commonly ulcer-cancers, local carcinomatous ulcer, and occasionally a scirrhus or a polyp. Sometimes the pain is spasmodic or colicky, as if the stomach were attempting to expel the growth.

The importance of recognizing this syndrome in gastric carcinoma lies in the fact that the treatment of uncomplicated duodenal ulcer is medical and that such measures afford relief in carcinoma by diminishing the associated gastritis. Only 8 of the 14 examples of this syndrome in my series were resectable.

Chronic atrophic antral gastritis is another condition which simulates duodenal ulcer during an exacerbation, but it may also show some of the features of a carcinoma, as there may be anorexia, loss of weight, achlorhydria, and occasionally occult blood and some anaemia. Considerable attention is being centred upon this condition to-day as the result of cytological studies, and its position as a premalignant state is attracting a fresh study, as are the works of Konjetzny, of Hurst, and of Faber, who propounded this view nearly 30 years ago. The need to investigate patients carefully with this syndrome requires no further argument.

Combined Dyspepsias.—In the later stages of the disease some patients complain of both a filling and an emptying dyspepsia. There is usually some immediate symptom on eating, such as nausea, fullness, or discomfort eased by belching, by alkalis, or by vomiting; an hour or two later the patient complains of a hunger pain, for which he feels he must eat. When he does the cycle of dyspepsia starts over again. He is therefore apt to complain that he gets pain with or without food—or at any time. There were six examples of this combination in the series: two leather-bottle stomachs; two diffuse carcinomas of pyloric antrum and body; one diffuse carcinoma of lesser curve accompanied by a malignant polyp on the greater curvature; and one localized scirrhus in the pyloric canal. It will be noted that in the last condition encroachment upon the pyloric sphincter set up both a filling and a duodenal type of dyspepsia and that in the other five instances the growths were extensive.

Obstructive Syndromes

Obstructive lesions are never found in the early stages of the disease. Stenosis at the pylorus or cardia may certainly develop insidiously, but in the majority there is a prodromal dyspepsia. Where such is absent the first sign of obstruction may be an attack of vomiting, and this should always receive particular attention. Visible peristalsis in the epigastrium should be looked for, and a lump may be felt. In the series there were eight examples of pyloric stenosis and five were resectable.

Dysphagia is usually described as the cardinal symptom of stenosis at the cardia. This is misleading. In 17 examples only seven patients complained initially of dysphagia; in nine there was a preliminary dyspepsia lasting from 3 to 12 months; and one had had stomach trouble for five years before his dysphagia appeared. Two patients were admitted with haematemesis, two had troublesome hiccup, and one had a fixed pain in the left hypochondrium. In no case had the growth extended down from the lower oesophagus, though this of course is a possibility. The lesson is that the cardia may become stenosed by a growth at that site or by the upward extension of a growth from the neighbouring parts of the stomach.

In hour-glass stenosis and in linitis plastica pain and the regurgitation of food may also follow in the course of a meal. It is therefore necessary to know whether the lesion is in the lower oesophagus, the cardia, or the upper part of the stomach and whether the oesophageal wall is free from secondary deposits. Cardiac growths appear to be relatively favourable for surgery so long as the liver and oesophagus are not involved. Eleven of the 17 cases were found to be operable. They appear to be of the less-malignant types. In a recent experience a local recurrence in the lower oesophagus four years after a total gastrectomy proved to be resectable.

Other Symptoms

Unusual symptoms may lead the clinician astray. Pains referred from the stomach posteriorly should not be mistaken for muscular strain or rheumatism or spinal arthritis. Pains referred to the left or right flank having a close relation to food should not be confused with pain originating in the colon simply because there is increasing constipation. Colicky spasms originating in the stomach spread from left to right and should be distinguished from those of the transverse colon. A fixed pain in the left hypochondrium which is aggravated by food is not of renal origin. It is usually gastric and calls for investigation. Persistent hiccup may be a significant symptom.

Physical Signs

Wasting and anaemia, gastric peristalsis in pyloric stenosis, and the possible presence of an epigastric lump are all the physical signs that may be found in operable cases. The mobility of the gastric tumour is important, but of course only those in the lower half of the stomach can be felt. This may be difficult if the stomach is empty, but with a full stomach it may be easier, particularly on deep inspiration or with the patient erect. The lump of an early carcinoma is usually painless on palpation and so differs from the "ulcer-tumour" of a chronic peptic ulcer, which is tender and may diminish in size under medical treatment within a few weeks.

The odd patient may be encountered who announces that he has a lump in his stomach but no other complaints. The prognosis need not be hopeless, for 27 out of 50 palpable carcinomas were found to be operable.

Signs of Dissemination

Epigastric tenderness and guarding generally mean peritoneal involvement in the gastric field, and all the other physical signs found later in the disease arise from its dissemination. These include: (1) Distant lymphatic metastases—in the left supraclavicular region, the left axilla, or groins. (2) Liver enlargement from secondary deposits or with obstructive jaundice from lymphatic metastases in the portal fissure. (3) Transperitoneal pelvic deposits found on rectal examination: (*a*) the rectal shelf of Shenton or (*b*) Krukenberg's bilateral ovarian tumours. (4) Ascites or left pleural effusion. (5) Carcinomatosis peritonei with or without intestinal obstruction. (6) The hard umbilical nodule or other skin nodules. (7) Pyrexia from widespread disease. (8) Cachexia—possibly with diarrhoea. (9) The secondary involvement of other organs such as lung, bone, spine, and brain.

Associated Gastric Lesions

A brief glance at the records of those with long histories shows that, whilst in some the carcinoma may have developed slowly, in others there is an interesting background of previous stomach trouble in which there has often been a recent change in the symptoms. Such patients include cases of gastric and duodenal ulcer, of recurring gastritis with or without bleeding, or haematemeses treated at home, of gastro-enterostomy for duodenal ulcer, and of recurrent

carcinoma in the gastric stump—the occurrence of such cases 3½, 7, and 17 years after a partial gastrectomy for cancer suggests a new malignancy.

In addition there were cases with a double pathology such as gastric or duodenal ulcer with carcinoma; chronic gastritis, simple polyp and cancer; simple and malignant polyp; and malignant polyp and infiltrating carcinoma. These lend force to the dictum of Hurst that gastric carcinoma never develops on a normal mucosa.

Conclusion

The emphasis in an earlier clinical diagnosis is upon symptoms, and the taking of a careful clinical history is the first step. Once the suspicion of malignancy is aroused in the mind of the surgeon and investigations are begun, he must be wary of the negative report, for this in the past has led to disaster. Fortunately he can now rely upon three lines of scientific investigation—namely, radiology, gastroscopy, and cytology—and by sifting the evidence they provide he may reasonably hope to advance the detection of this disease and thereby to improve the prospect of cure which only surgery can offer.

PROSTATITIS AND ANKYLOSING SPONDYLITIS

BY

R. M. MASON, D.M., M.R.C.P.
R. S. MURRAY, M.D., F.R.C.S.I., D.M.R.
J. K. OATES, M.B., B.S., M.R.C.P.Ed.

AND

A. C. YOUNG, M.B., B.S., D.M.R.D.
From the London Hospital

As part of a study of the radiological appearances of Reiter's disease two groups of patients, one with ankylosing spondylitis and one with rheumatoid arthritis, have been used for comparison. Since it has been argued that (1) Reiter's disease is a variant of rheumatoid arthritis (Littler, 1951), (2) ankylosing spondylitis is a variant of rheumatoid arthritis (Committee of American Rheumatism Association, 1953), (3) ankylosing spondylitis is a complication of Reiter's disease (Ford, 1953), and (4) ankylosing spondylitis is due to genital infection (Romanus, 1953), it was clearly necessary to determine the incidence of genital inflammatory disease in the two latter groups. All cases were therefore examined for signs of chronic prostatitis. We were impressed with the frequency with which patients with ankylosing spondylitis were found to have this condition when compared with those suffering from rheumatoid arthritis, the incidence being almost as high as that found in patients with Reiter's disease. We have therefore examined the data with particular care to ensure that this finding is not due to some other unrelated factor or to misdiagnosis. The present report covers this part of the investigation alone, and the radiological findings are discussed only to the extent that they relate to this aspect.

Clinical Material

Fifty-four cases of ankylosing spondylitis were studied and compared with 86 cases of rheumatoid arthritis and 59 of Reiter's disease, all males, a total of 199 cases. Those with ankylosing spondylitis and rheumatoid arthritis presented to the Department of Physical Medicine and Regional Rheumatism Centre of the London Hospital, and those with Reiter's disease mostly to the Whitechapel Clinic. We have included in the ankylosing spondylitis group only those cases in which a confident clinical diagnosis had been made, and have excluded all those in which reasonable doubt existed—for example, cases which might be classified as atypical spondylitis by Sharp and Easson (1954) and Sharp (1957). All the patients with rheumatoid arthritis were well-established typical cases. The diagnosis of Reiter's disease was based on the finding of a non-gonococcal urethritis associated with an arthritis of acute onset and a variable, often chronic, relapsing course. Conjunctivitis occurred in 24 of the 59 cases (40%) and uveitis and keratodermia blennorrhagica in 6 cases (10%) each.

Age Distribution and Disease Duration.—Each group presented a distinct frequency distribution of age at the time of study (Table I), the mean age of the ankylosing spondylitis group being 37.4 years, with a mean duration of disease of 10.1 years; the rheumatoid arthritis group had a mean age of 52.7 years, with a mean duration of 6.7 years; and the Reiter's disease group a mean age of 42.2 years, with a mean duration of 8.4 years. Disease duration was estimated from the first joint or spinal symptom in all categories.

Rose–Waaler Test

A Rose–Waaler test was carried out in 80% of the ankylosing spondylitis group, in all but one of the patients with rheumatoid arthritis, and in 34% of those with Reiter's disease. The technique used was that originally described by Waaler (1940) and Rose *et al.* (1948). Later modifications have given a higher degree of sensitivity to this test, but were not used for this study because of the additional time required for these techniques, time which a laboratory in a general teaching hospital could not allocate. The results (Table II) do, however, show a clear distinction between the rheumatoid arthritis group on the one hand and the ankylosing spondylitis and Reiter's disease groups on the other. 35% of the rheumatoid arthritis group (38% of those with a history of one year or more) gave a positive Rose–Waaler test at the 1/16 level, while there were no positive titres in the other two groups. The incidence of positive tests in the rheumatoid group is comparable to that of Miller *et al.* (1949), who obtained 33%, using a similar technique. An analysis of the sample of ankylosing spondylitis and of Reiter's disease on which the test was done shows that these were reasonably homogeneous samples in terms of disease duration, the mean duration of the ankylosing spondylitis sample being 10.0 years and of Reiter's disease 6.2 years.

TABLE II.—*Results of Rose–Waaler Test*

	Positive		Negative		Test Not Done	
	No.	%	No.	%	No.	%
Ankylosing spondylitis ..	0	0	43	80	11	20
Rheumatoid arthritis	30	35	55	64	1	1
Reiter's disease	0	0	20	34	39	66

TABLE I.—*Clinical Material—Age at Time of Study*

	Age in Years												Total	Mean Age (Years)	Mean Duration (Years)	Mean Age of Onset (Years)
	15–		25–		35–		45–		55–		65–					
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%				
Ankylosing spondylitis ..	9	17	10	19	25	46	6	11	4	7	0	0	54	37·4	10·1	27·3
Rheumatoid arthritis ..	0	0	5	6	15	17	29	34	26	30	11	13	86	52·7	6·7	46·0
Reiter's disease	6	10	12	20	11	19	25	42	4	7	1	2	59	42·2	8·4	33·8

Sacro-iliitis

As part of the radiological survey the sacro-iliac joints of all patients were radiographed. Seven of the films (four Reiter's disease, two rheumatoid arthritis, and one ankylosing spondylitis) were not available at the time of reading, leaving 192 *x*-ray films for analysis. All were read "blind"—that is, without knowledge of the clinical diagnosis—by two of us, one a clinician, the other a radiologist. Only those findings referring to the sacro-iliac joints are reported on here. Equivocal changes were recorded, since we felt that early or slight changes might be missed if they were not. In the event these do not appear to alter the picture significantly. The three disease categories are distinctive (Table III).

TABLE III.—*Incidence of Radiological Sacro-iliitis*

	Ankylosing Spondylitis	Rheumatoid Arthritis	Reiter's Disease
Unequivocal bilateral sacro-iliitis	49 (94%)*	7 (8%)*	19 (32%)*
Equivocal bilateral sacro-iliitis	1	6	2
Unequivocal unilateral sacro-iliitis	1	12	6
Equivocal unilateral sacro-iliitis	0	9	4
No sacro-iliitis	2	50	24
X-ray films not available	1	2	4
	54	86	59

* These percentages are calculated assuming that the non-available films were normal.

Unequivocal bilateral sacro-iliitis was recorded in 49 of the 54 (91%) of patients with ankylosing spondylitis, normal sacro-iliac joints being found in only 2 cases. This is approximately the expected incidence (Thompson, 1957), bearing in mind the fact that, for reasons of economy, special techniques (Grainger, 1957) were not used. In the rheumatoid arthritis group unequivocal bilateral sacro-iliitis was present in 7 of 86 cases (8%) of those radiographed, an incidence similar to that found by Sharp (1957). In Reiter's disease the figures are intermediate, bilateral sacro-iliitis being recorded in 19 of 55 cases (35%).

Prostatitis

All the patients in the rheumatoid arthritis and ankylosing spondylitis groups (with the exception of one patient with rheumatoid arthritis who refused examination) were examined by one of us (J. K. O.) for the presence of chronic prostatitis, using a standard technique. Five samples of the fluid obtained by prostatic massage were scrutinized by dark-field microscopy for the presence of polymorphonuclear leucocytes in clumps. The diagnosis of chronic prostatitis (or more correctly "prostato-vesiculitis," as the expressed fluid is usually a mixture of vesicular and prostatic fluids) was made only on the finding of pus cells in clumps, with a minimum of 10 pus cells per high-power field. In nearly all cases very many more than 10 pus cells per field were found; indeed, the average clump usually comprised between 30 and 50 cells (Fig. 1). No distinctive features were found in the pathological appearances of the prostatic fluids in positive cases, whichever group the specimen was obtained from. These criteria for the diagnosis of chronic prostatitis are generally accepted (Hinman, 1935; Pelouze, 1939); also, as repeated massage was not practicable, our results represent the minimum incidence, and the true figures are probably higher. In the patients with Reiter's disease all except four had non-specific urethritis. These four gave a clear history of urethral discharge which had ceased at the time of examination. The prostatic fluid, which was examined in each case after the acute phase of the disease was over, was found to be normal in all four patients.

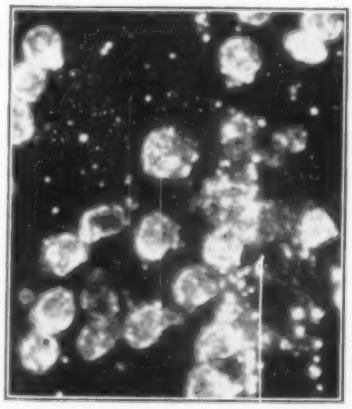

FIG. 1.—Typical positive prostatic smear (portion of 1/12 field).

Table IV gives the overall incidence of prostatitis in the three groups.

TABLE IV.—*Incidence of Prostatitis*

	Prostatitis		No Prostatitis	
	No.	%	No.	%
Ankylosing spondylitis	45	83	9	17
Rheumatoid arthritis*	28	33	57	67
Reiter's disease	56	95	3	5

* One refused.

The difference between the ankylosing spondylitis group, with an incidence of 83% prostatitis, and the rheumatoid arthritis group, with 33%, is highly significant ($P<0.01$). The high incidence in the Reiter's disease group is not surprising. The incidence in the ankylosing spondylitis group is similar to that reported by Romanus (1953), who, in a very careful study of 117 cases without, however, any controls, found an incidence of "prostato-vesiculitis" in 102, or 91%. His slightly higher figures may be accounted for by the very detailed investigation carried out in each case.

The difference between the rheumatoid arthritis and ankylosing spondylitis groups in respect of the incidence of prostatitis requires further analysis and consideration of whether this could be due to differences other than the disease process itself. Is it possible, or likely, that the difference in the ages of the two groups is the operative factor? The mean age of the rheumatoid arthritis group is some 15 years more that that of the spondylitis group (Table I), with a maximum incidence in the 45–64 decades, while the ankylosing spondylitis group has a maximum incidence in the 35–44 decade. Can it be argued that prostatitis in the younger and more sexually active male is commoner than in the older age group? Other control studies — for example, Parrino (personal communication) — suggest the opposite. He found an incidence of 38% prostatitis in a group of 411

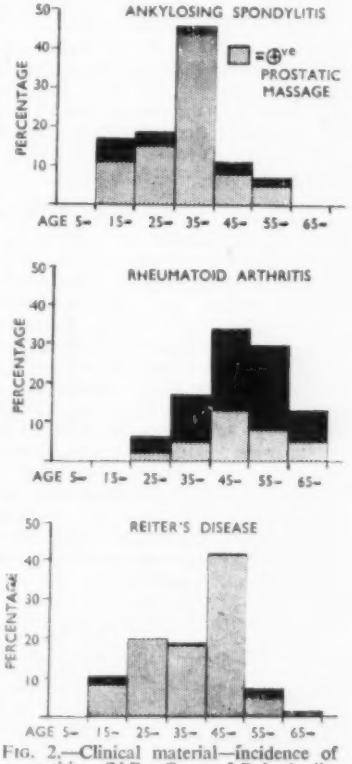

FIG. 2.—Clinical material—incidence of prostatitis. (N.B. Cases of Reiter's disease with frank non-specific urethritis are included in the positive massage group.)

recruits, and he also examined 129 normal civilians. Of the latter, 30% had chronic prostatitis and there was a positive correlation with increasing age.

Table V and Fig. 2 show the correlation between age and prostatitis in the present material. It will be seen that the pattern of prostatitis in the ankylosing spondylitis group follows almost exactly the pattern of age distribution of the group. Moreover, the incidence in the rheumatoid arthritis group shows no trend in favour of the younger decades. On the contrary, of the 15 cases of rheumatoid arthritis in the 35–44 decade, only 4 had prostatitis, an incidence of 27%, or less than the incidence for the whole group; whilst in the same decade in the ankylosing spondylitis group 24 of the 25 cases (96%) had prostatitis. It seems unlikely, therefore, that the difference results from differences of age.

A similar examination of the relation of prostatitis to disease duration revealed no trend in favour of any relationship between duration of disease and prostatitis such as could account for this finding.

Prostatitis in Rheumatoid Arthritis

Control data, to be valid, must be obtained from a population of the same age and by using the same technique—indeed, the same individual carrying out the examination, since skill will be a variable. Adequate figures are thus hard to obtain. Ambrose and Taylor (1953) found 25% of young normal males to have chronic prostatitis. Oates (1957) found 20% of 63 males between the ages of 18 and 45 similarly affected. The rheumatoid arthritis group may, however, form a fairly satisfactory control group. It is necessary to be sure that it does not contain cases of Reiter's disease or of ankylosing spondylitis misdiagnosed as rheumatoid arthritis, since these will tend to give a falsely high incidence of prostatitis. If, however, there were a number of cases of Reiter's disease or ankylosing spondylitis in this group then we should expect to find a higher incidence of prostatitis in the cases with a negative serology.

In the event an exactly similar incidence was found in both groups (33%), which would support the supposition that no substantial error arises from this cause. It seems probable that the incidence of prostatitis, as judged by our criteria, in the rheumatoid arthritis group represents a fair approximation of that to be found in the general population of similar age distribution from which the clinical material was drawn.

Sacro-iliitis and Prostatitis

The incidence of sacro-iliitis is higher in Reiter's disease than in rheumatoid arthritis (Table III). In the present series, 35% had unequivocal bilateral sacro-iliitis. In those with a history of over five years it reached 61%. This has been commented on previously by others (Marche, 1950, 1954; Sharp, 1957), although Harkness (1949, 1950) found an incidence of only 5%. We have therefore examined our material to see whether there could be any association between sacro-iliitis as such and prostatitis. The number of cases with no evidence of prostatic disease is small, except in the rheumatoid arthritis group, where the incidence of sacro-iliitis was not significantly different whether prostatitis was present or not. All 11 cases of ankylosing spondylitis with a normal prostatic fluid had unequivocal bilateral sacro-iliitis, but none of the four cases of Reiter's disease with a normal prostatic fluid had changes in the sacro-iliac joints.

Alternatively, is it possible that prostatitis follows or results from sacro-iliitis? If so, one would expect the incidence of prostatitis to be higher amongst cases with sacro-iliitis. Of the 49 cases of ankylosing spondylitis with unequivocal bilateral sacro-iliitis, 38 (79%) had prostatitis, compared with an incidence in the whole group of 83%. In the rheumatoid arthritis group two out of six (33%) had prostatitis, compared with 33% in the whole group. If prostatitis resulted from sacro-iliitis one would have expected a higher incidence in these cases; the figures do not suggest that this is likely.

Age of Onset of Symptoms

Five cases of ankylosing spondylitis, or 9%, had their first joint or spinal symptom at the age of 14 or before—three at the age of 14, one at 13, and one at 12. A prepubertal onset has been noted by others (Polley and Slocumb, 1947; Lennon and Chalmers, 1948; Simpson and Stevenson, 1949; Lucchesi and Lucchesi, 1950; Romanus, 1953; Baird *et al.*, 1955). Hart's (1955) series of 184 cases contained 16 males whose onset was between the age of 10 and 15 years—an identical incidence of 9%.

These figures are clearly of some importance when considering the relationship of genito-urinary infection to ankylosing spondylitis. It must be noted that the date of onset in these cases may well be from the beginning of peripheral joint involvement rather than sacro-iliitis, which is difficult to observe at this age; and Ziff *et al.* (1956) draw attention to the incidence of spondylitis in post-pubertal patients with rheumatoid arthritis of juvenile onset. Of the five cases in the present series, three had prostatitis. These were those with long-standing disease—20, 20, and 21 years—whilst the two with five and seven years' duration had normal prostates.

Past History of Venereal Disease

In view of the possibility that the higher incidence of prostatitis in the ankylosing spondylitis group was due to a higher incidence of previous venereal infection, all patients were questioned closely about previous venereal disease. As might be expected, this was high in the Reiter's disease group: 27 of the 59 cases (46%) had had a previous attack of gonococcal urethritis, while the incidence in the ankylosing spondylitis group and rheumatoid arthritis group was low—5 of 54 (9%) in the former, and 4 of 86 (5%) in the latter. All the ankylosing spondylitics with a past history of urethritis had chronic prostatitis. In the rheumatoid arthritis group only two had prostatitis.

Discussion

The association between prostatitis and ankylosing spondylitis is not a new finding. The literature has been very fully reviewed by Romanus (1953), who points out that it goes back at least to 1926, when Marie amended his original paper of 1898 to the effect that the gonococcus was responsible for spondylitis; and many other workers since then—for example, Forestier (1935, 1939) and Volhard (1938)—have reported on the association between venereal infection and spondylitis. Others—for example, Watson-Jones and Osmond-Clarke (1955) and West (1949)—have contested this view. Much of the work is, however, obscured by a failure to distinguish between Reiter's disease with a subsequent spondylitis and ankylosing spondylitis itself, a distinction which is often by no means easy in

TABLE V.—*Age Distribution of Prostatitis*

	Age in Years												Total	Mean Age (Years)	Mean Duration of Arthritis (Years)
	15–		25–		35–		45–		55–		65–				
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%			
Ankylosing spondylitis	6	11	8	15	24	44	4	8	3	5	0	0	45	37·8	10·7
Rheumatoid arthritis	0	0	2	2	4	5	11	13	7	8	4	5	28	52·5	6·8
Reiter's disease	5	8	12	20	10	18	25	42	3	5	1	2	56	42·1	9·0

individual cases. We have, however, been impressed by the contrast between Reiter's disease occurring in a slightly older age group—presenting with what is often, although not always, a florid urethritis and acute peripheral arthropathy and with a slowly developing, clinically silent sacro-iliitis—and ankylosing spondylitis with early sacro-iliitis, and, usually, an asymptomatic genital infection.

The evidence regarding whether prostatitis is an associated phenomenon or aetiologically related to ankylosing spondylitis is still not clear, and the interpretation of the data remains difficult. It is well recognized that chronic prostatitis may exist even when examination of a specimen of prostatic fluid may show few or no inflammatory cells. The explanation usually offered is that fibrosis or pocketing of inflammatory exudate takes place and that these areas may not be opened and drained by a first massage. This could explain some of the negative findings in the nine patients with ankylosing spondylitis. The finding of a normal prostatic fluid in the four patients with Reiter's disease who also had normal sacro-iliac joints is of little significance, since it is clear that the disease is quite often cured and no evidence of genital disease remains. In the rheumatoid arthritis group there is no correlation between sacro-iliitis and genital inflammatory disease. The opposite is the case when the findings in ankylosing spondylitis are considered. There is, however, no proof that the genital inflammation causes sacro-iliitis as postulated by Romanus, although it must be admitted that this is a seductive hypothesis, and the high incidence of sacro-iliac disease in male paraplegics (Abramson and Kamberg, 1949; Abel, 1950), nearly all of whom can be expected to have chronic prostatitis (Prather, 1949), adds support to such a theory. That many patients have apparently identical genital inflammatory disease in the form of chronic prostatitis and never develop sacro-iliitis is obvious. Many explanations could be offered for this—for example, the prostatitis producing sacro-iliitis may be due to a specific, so far unidentified, organism. This might cause sacro-iliitis in all patients so infected, or perhaps in only those genetically predisposed. Conversely, the cause of the prostatitis may be a single one which operates to produce sacro-iliitis only in those patients with a suitable genetic background. The importance of genetic factors in ankylosing spondylitis is, of course, well recognized (Tegner and Lloyd, 1949; West, 1949; Hersh *et al.*, 1950; Mason, 1951; Graham and Uchida, 1957). Genetic studies of Reiter's disease have not, so far as we are aware, been carried out, although a few families have been reported (Koster and Jansen, 1946; Trier, 1950; Fabregoule, 1951; Csonka, personal communication, 1957). One of our series with the full syndrome had a brother who appeared to have suffered an identical attack, but he refused to attend for examination. It seems clear, therefore, that until the organism responsible for non-specific urethritis is identified, cause and effect cannot be distinguished, and no more than an association between ankylosing spondylitis and inflammatory disease of the genital tract can be established.

Summary

The incidence of chronic prostatitis in 54 cases of ankylosing spondylitis is described and compared with the findings in 59 cases of Reiter's disease and 86 of rheumatoid arthritis.

The high incidence of chronic prostatitis in ankylosing spondylitis is discussed.

It is concluded that there is a real association between ankylosing spondylitis and inflammatory disease of the urogenital tract.

We would like to record our gratitude to Mr. Ambrose King for his helpful interest and valuable criticisms, and to Dr. H. B. May and Dr. J. Perrin and their staff for carrying out the serological tests.

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The Government of India has published a report by S. C. Seal and L. M. Bhattacharji on a health survey undertaken in Sikkim State by the section of epidemiology of the All India Institute of Hygiene and Public Health, Calcutta. The main purpose of the survey was to obtain an integrated picture of health and sickness in the community studied, and the work consisted of physical examination of individuals, the recording of family data and medical and social histories, the collection and examination of laboratory specimens, insects, and rodents, and the assessment of environmental and socio-economic conditions. Sikkim lies between Tibet in the north and Darjeeling District in the south and has a population of nearly 150,000. The majority of the people are ignorant about the causes or prevention of disease, being demonistic or deistical in outlook on health matters. They are reluctant to keep themselves clean, and pediculosis, scabies, and worm infestation are very widespread. The almost universal drink of the people is rakshi, a kind of alcohol prepared from fermented millet or buckwheat. Next to alcohol the common addiction is tobacco; even among children 12% indulge in alcohol and 15% in tobacco. In addition, 1.2% of the population indulge in opium. The rate of marriage was least among the Christians and highest among the Hindus, with the Buddhists occupying an intermediate position. There are no official vital statistics, but those carrying out the survey estimated the crude birth rate to be 28.8 per 1,000 and the crude death rate 15.9 per 1,000. The abortion and stillbirth rates were 9.1% and 3.6%, respectively. The infant mortality rate was 208 per 1,000. As a result of the survey, certain measures have been suggested to overcome the main health problems that were found to be seriously affecting the economy of the State.

A HAEMOGLOBINOPATHY INVOLVING HAEMOGLOBIN H AND A NEW (Q) HAEMOGLOBIN

BY

F. VELLA, M.D., B.Sc., B.A.(Oxon)
Department of Biochemistry, University of Malaya, Singapore

R. H. C. WELLS, M.B., B.Sc., M.R.C.P., D.M.T.&H.
Department of Medicine, General Hospital, Singapore

J. A. M. AGER, M.B., B.S.
Jenner Laboratory, St. Thomas's Hospital, London

AND

H. LEHMANN, M.D., Ph.D., Sc.D., F.R.I.C.
Department of Pathology, St. Bartholomew's Hospital, London

The technique of electrophoresis was first used successfully in the study of adult haemoglobin by Pauling, Itano, Singer, and Wells (1949), when they demonstrated that haemolysates obtained from the erythrocytes of patients suffering from sickle-cell anaemia exhibited properties which differed greatly from those of haemolysates of erythrocytes from normal adult individuals. This discovery of the usefulness of electrophoresis in the study of haemoglobin has led to the recognition of other variants of adult human haemoglobin, whose genetic control, somatic effects, and geographical distribution have been under intensive study ever since.

It is the purpose of the present communication to describe in detail the properties of a new haemoglobin which was detected in association with haemoglobin H and to give the clinical and other findings in the patient presenting this new haemoglobinopathy.

Case Report

A Chinese man aged 24 was first admitted to the general Hospital, Singapore, in August, 1953, with a history of shortness of breath, palpitations, giddiness, blurring of vision, and precordial pain on exertion, associated with anorexia and generalized oedema. The onset of these symptoms had been insidious over a period of about three months.

He was found to have a gross hypochromic anaemia, haemoglobin 2.9 g./100 ml., with *Ancylostoma* ova in his stools. Following blood transfusion, treatment with iron, and worming he quickly improved, and when his haemoglobin level was 10.2 g./100 ml. he was discharged. One year later, in September, 1954, he was readmitted with similar but less severe symptoms, a haemoglobin of 5.1 g./100 ml., and again *Ancylostoma* ova in his stools. He was again wormed and treated with iron. When his haemoglobin reached 9.9 g./100 ml. he was again discharged, and has since been followed continuously as an out-patient. Although there has been no recurrence of his ancylostomiasis, his haemoglobin varies between 3.6 and 11.8 g./100 ml. Treatment with large doses of iron by injection and by mouth, with vitamin B_{12}, folic acid, ascorbic acid, and multiple vitamin preparations, has failed to produce any response.

A recent examination showed him to be a pale, listless, slim young man, with slight sternal tenderness. There were no other abnormal physical signs, and in particular he had no enlarged lymph nodes and his liver and spleen were not palpable. He was not jaundiced.

Radiological Investigations.—Chest radiographs showed no abnormality, but radiographs of the skull showed about 12 small radiotranslucent areas, mostly in the parietal regions (Fig. 1). These areas have a diffuse outline, are roughly circular, and vary from 4 to 11 mm. in diameter. The diploë of the skull were normal. Radiographs of the hands showed small sharply defined radiotranslucent areas in the distal shafts of all the proximal and middle phalanges and also in the bases of both second metacarpals (Fig. 2). Otherwise the bony trabeculae of both hands appeared to be within normal limits. Radiographs of the feet showed similar radiotranslucent areas in the phalanges.

FIG. 2.—Radiograph of hand showing radiotranslucent areas in phalanges and second metacarpal.

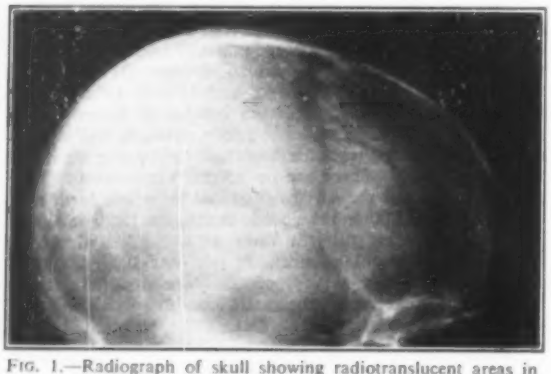

FIG. 1.—Radiograph of skull showing radiotranslucent areas in parietal region.

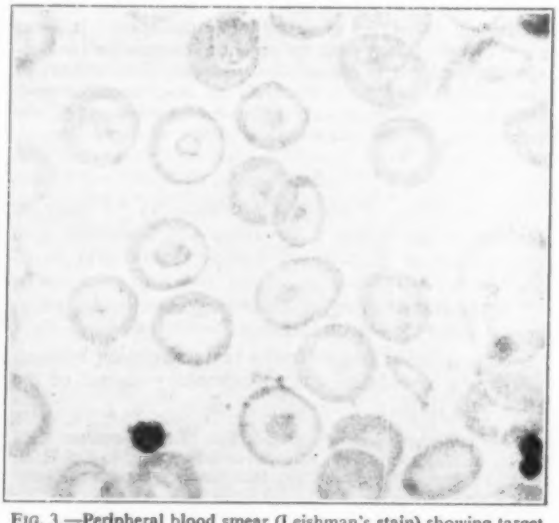

FIG. 3.—Peripheral blood smear (Leishman's stain) showing target cells.

Laboratory Investigations.—Blood Wassermann, Kahn, and V.D.R.L. tests were negative. Serum bilirubin was 0.6 mg./100 ml.; serum iron, 220 μg./100 ml.; urine urobilinogen, 16 mg. in 24 hours; faecal urobilinogen, 320 mg. in 24 hours. The urine contained no albumin, sugar, or acetone, and the deposit was normal on microscopy. The stools contained no amoebae, cysts, or ova. A histamine test showed a normal gastric hydrochloric acid response. The haematological investigations showed: haemoglobin, 10.1 g./100 ml.; R.B.C., 4,810,000/c.mm.; P.C.V., 43.4%; M.C.V., 90.2 cubic microns; M.C.H., 21.0 μμg.; M.C.H.C., 23.3%; M.C.D., 7.7–7.8 μ (halometry); W.B.C., 8,100/c.mm. (neutrophils 68%, lymphocytes 23%, eosinophils 5%, monocytes 4%); thrombocytes 278,000/c.mm.; reticulocytes 8%.

A peripheral blood film stained with Leishman's stain showed moderate hypochromia, anisocytosis, poikilocytosis, polychromasia, and many target cells (Fig. 3). The leucocytes and platelets appeared normal. Supravital staining with brilliant cresyl blue showed inclusion bodies (Fig. 4) in about 95% of the erythrocytes, as is seen in blood which contains haemoglobin H. Resistance to lysis

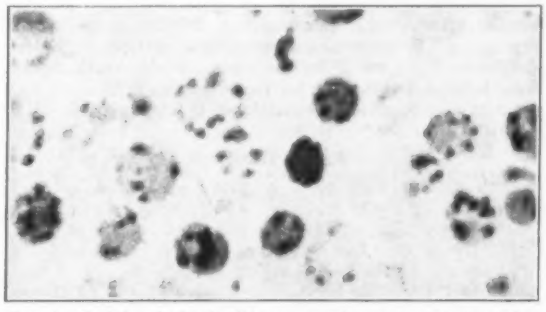

FIG. 4.—Peripheral blood. Wet preparation. Supravital staining with brilliant cresyl blue. Note the inclusion bodies.

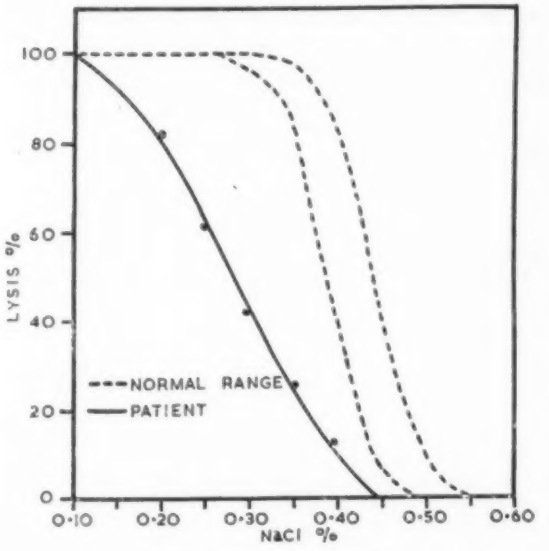

FIG. 5.—Osmotic fragility.

by hypotonic saline was increased, haemolysis began at 0.45% NaCl and was complete only at 0.10% NaCl (Fig. 5). There was no sickling with 2% sodium metabisulphite and there were no siderocytes. Direct and indirect Coombs tests were negative at 4° C., 20° C., and 37° C.

Investigation of the Haemoglobin

Paper electrophoresis at *p*H 8.6 showed two components on every occasion that fresh blood samples were examined. The smaller, comprising 20% of the total, had the mobility of haemoglobin H or I, and the remainder moved between haemoglobins A and S. At *p*H 6.5 the smaller fraction moved towards the anode, which is the unique property of haemoglobin H, and the remainder moved towards the cathode. This is the fifteenth instance of haemoglobin H seen in Singapore, most of the subjects being of Chinese extraction. No alkali-resistant haemoglobin was found, and the haemoglobin A_2 fraction was not increased.

A sample of the haemoglobin was sent to Dr. Lie-Injo Luan Eng, of the University of Indonesia, Djakarta, and she found that the non-haemoglobin H component had a mobility resembling, but slightly differing from, that of haemoglobin S. It differed from her recently observed Buginese "X" component (Eng, 1956, 1957).

The following haemoglobins move on paper electrophoresis at *p*H 8.6 between A and S in order of mobility: F, G, and L. The non-haemoglobin H component moved more slowly than haemoglobin F; unlike F, it was not

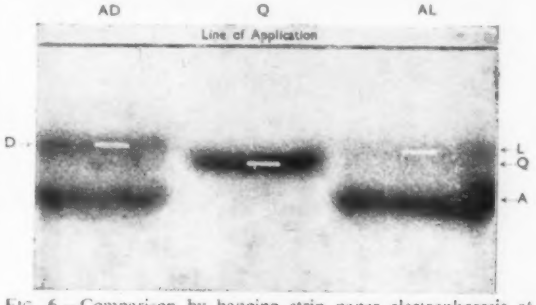

FIG. 6.—Comparison by hanging strip paper electrophoresis at *p*H 8.6 of haemoglobins A plus D and A plus L with the non-H haemoglobin of the patient. The new haemoglobin moves faster than haemoglobins D and L but more slowly than haemoglobin A. White lines mark centre of density of bands A + D, Q, and A + L.

resistant to alkali-denaturation, and when mixed with haemoglobin A it separated clearly from this haemoglobin, whereas no such separation can be achieved between haemoglobins A and F on paper electrophoresis at alkaline *p*H. The non-haemoglobin H component moved in advance of haemoglobin L (Fig. 6), and most resembled haemoglobin G in its position. However, there was a slight difference in that the new compound was moving a fraction faster than haemoglobin G (Fig. 7)—not unlike the haemoglobin described by Schwartz and Spaet (1955). The American authors decided that such a slight difference in mobility should not be taken into account for the time being, and called their haemoglobin G (Schwartz, Spaet, Zuelzer, Neel, Robinson, and Kaufman, 1957). In the comparison of the new haemoglobin by itself with a haemoglobin AG mixture the difference between the new haemoglobin and haemoglobin G was barely noticeable. But if the new haemoglobin by itself was compared with pure haemoglobin G, or if haemoglobin A was added to it and the resulting mixture was compared with a mixture of haemoglobin A plus G,

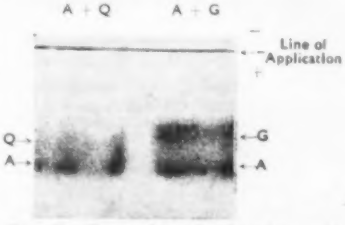

FIG. 7.—Comparison by hanging strip paper electrophoresis at *p*H 8.6 of a mixture of the new haemoglobin with haemoglobin A with haemoglobins A plus G. Note that the new haemoglobin moves slightly faster than haemoglobin G.

the fact that it moved faster than haemoglobin G became more obvious. The explanation for this is that pure haemoglobin G moves on paper electrophoresis at alkaline *p*H a little more slowly than the haemoglobin G of a haemoglobin A plus G mixture. In such a mixture the position of the separated G is just in front of that of pure haemoglobin G —that is, it is found a little nearer to the haemoglobin A fraction. This interaction between haemoglobins which move very similarly on electrophoresis is not unusual. For example, when a haemoglobin A plus J mixture is compared with pure haemoglobin A, the haemoglobin A of the mixture moves a little faster than the pure haemoglobin A.

Fortunately we were able to differentiate the present haemoglobin more definitely from haemoglobin G by ion-exchange-resin chromatography (Huisman and Prins, 1957). The following is the sequence of the haemoglobins in order of mobility by this technique: H, F, I (A–J–K), G, E (S–D), L, C. The new haemoglobin moved between haemoglobins S or D, and L. It was found close to L, but a mixture of the two divided and the new haemoglobin moved in advance of haemoglobin L (Fig. 8). On acid electrophoresis at

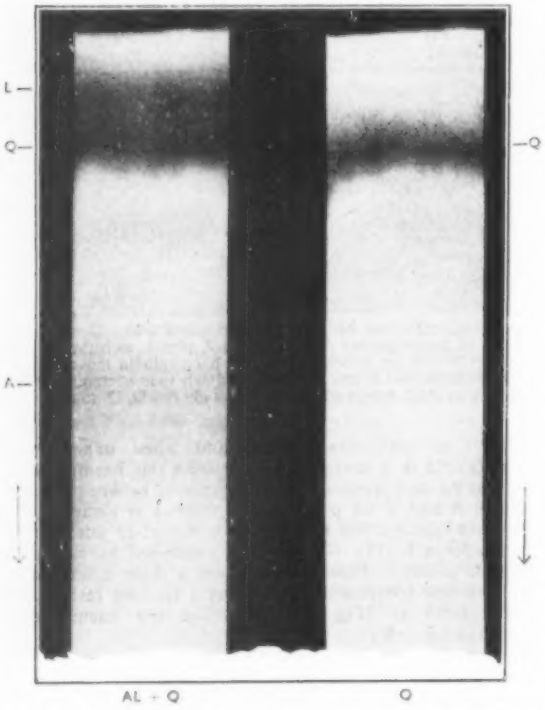

FIG. 8.—Comparison by ion-exchange chromatography between a mixture of haemoglobins A, L, and Q with haemoglobin Q only. It will be noted that haemoglobin Q moves similarly to haemoglobin L, but slightly in front of it. Upper two-thirds of columns shown.

*p*H 6.5 the compound resembled haemoglobin G in mobility, but on electrophoresis in agar at *p*H 6.2 (Robinson, Robson, Harrison, and Zuelzer, 1957) it resembled haemoglobin L and moved more slowly than haemoglobin S.

The solubility of the new haemoglobin was established after haemoglobin H had become denatured on storage in the cold and the precipitate had been removed by centrifugation. In Itano's (1953) solubility test the solubility of the new haemoglobin resembled that of haemoglobin G inasmuch as it was slightly lower than, or within the lower range of, the solubility of haemoglobin A. The solubility of the ferrohaemoglobin was 0.65 and 0.64 g. per litre of 2.58 *M* phosphate buffer. The visible and ultra-violet spectrum of the carboxyhaemoglobin showed no difference when compared with haemoglobin A.

The present case shows a haemoglobin which differs from all other known haemoglobins in its electrophoretic behaviour on paper electrophoresis at *p*H 8.6, although the difference from haemoglobin G is small. It also differs from all other known haemoglobins in its chromatographic behaviour, although it resembles haemoglobin L more than any other. The following haemoglobins are now known and named: A, C, D, E, F, G, H, I, J, K, L, M, and S. The letter N is for the time being reserved for a new haemoglobin from Liberia (Robinson, Zuelzer, Neel, Livingstone, and Miller, 1956). Two other abnormal haemoglobins have been described by Eng (1956, 1957), and by Schneider and Haggard (1957), which are provisionally known as Buginese X and the Galveston type respectively. The new haemoglobin has been compared with Liberia I and II, Buginese X, and the Galveston type haemoglobins, and has been found to differ from them all on paper electrophoresis at *p*H 8.6 and on resin-chromatography. One abnormal haemoglobin which moved faster than haemoglobin A on paper electrophoresis at alkaline reaction has been seen by Fessas and Papaspyrou (1957) in an infant shortly after birth, but it disappeared later on. It is therefore not yet certain whether this haemoglobin will come under the category of the inherited haemoglobin variants. Leaving the letters N, O, and P for the naming of the haemoglobins from Liberia, Indonesia, and Texas, we are calling the new pigment described here haemoglobin Q.

Family History

Both parents were born in Amoy of Hokien ancestry. They were not blood relatives. The father died as a young man. The mother was an only child and is alive in Singapore. There were five children, of whom two elder sisters are unavailable for study, having been last heard of from China in 1949. Two brothers died, aged 21 and 12, following a haematemesis and an undefined progressive illness respectively.

The patient's mother is about 60 years old and is totally deaf. Haematological investigations on her showed: haemoglobin, 11.7 g./100 ml.; R.B.C., 5,000,000/c.mm.; P.C.V., 36%; M.C.V., 72 cubic microns; M.C.H., 23.2 $\mu\mu$g.; M.C.H.C., 29.5%; M.C.D., 7.2 μ (halometry); W.B.C., 7,800/c.mm. (neutrophils 65%, lymphocytes 28%, eosinophils 4%, monocytes 3%); thrombocytes 275,000/c.mm.; reticulocytes, 1.3%. A peripheral blood film stained with Leishman's stain showed moderately hypochromic normocytic erythrocytes with minimal anisocytosis. Target cells were 1%. The leucocytes and platelets appeared normal. Supravital staining with brilliant cresyl blue showed no inclusion bodies. There was no sickling with 2% sodium metabisulphite. Siderocytes were absent. On paper electrophoresis at *p*H 8.6 she showed about 60% of haemoglobin A and about 40% of a haemoglobin resembling in mobility the non-haemoglobin H component of her son. Alkali-resistant haemoglobin amounted to 1%.

Haemoglobin Q–H Disease

Haemoglobin H was detected simultaneously in two Chinese siblings in America (Rigas, Koler, and Osgood, 1955, 1956) and in two Greek families (Gouttas, Fessas, Tsevrenis, and Xefteri, 1955). It has since been found in Filipinos (Motulsky, 1956), in Thais (Na-Nakorn and Minnich, 1956), in a Malay (Lehmann and Singh, 1956), in a Greek Cypriot (Ager and Lehmann, 1957), in a Trans-Jordanian (White, Beaven, and Ellis, 1956), in Chinese in Indonesia (Eng, Poey, Kho, and Endenburg, 1957), in Singapore (Vella, 1957), and in a Nepalese Gurkha in Singapore (Brain and Vella, 1958).

The haemoglobin H trait usually presents clinically as a moderate or severe hypochromic microcytic anaemia resistant to iron therapy, with or without splenomegaly, radiological changes, and target cells, the finding of intra-

erythrocytic inclusion bodies on supravital staining with brilliant cresyl blue, and a decreased erythrocyte osmotic fragility. The present patient's condition would have been diagnosed clinically as thalassaemia, though the marked and unusual radiological findings and the absence of splenomegaly would have aroused suspicion.

Whenever family studies have been possible haemoglobin H has not been found in the phenotype unless one of the parents had thalassaemia. It has been suggested by Rigas *et al.* (1956) and by Motulsky (1956) that the gene for haemoglobin H does not find expression unless the simultaneously present gene for haemoglobin A is modified by the additional inheritance of a thalassaemia gene.

We might speculate that our propositus inherited a gene for haemoglobin Q from his mother, and that the father transmitted a gene for haemoglobin H. Unlike haemoglobin A, haemoglobin Q would then not fully repress haemoglobin H in the non-thalassaemic haemoglobin H heterozygote. However, we have no evidence so far that haemoglobins A and H or haemoglobins Q and H are allelomorphs. Two of various possibilities are that the propositus inherited both genes for haemoglobins A and Q from his mother and a gene for haemoglobin H and one for thalassaemia from his father, or that he inherited one gene for haemoglobin Q from the mother and one for haemoglobin H and one for thalassaemia from the father. In either case the father would have suffered from haemoglobin H disease. If this were so, it would explain why the father died young and why two brothers of the propositus died prematurely. The condition described here may well turn out to be a haemoglobin H–thalassaemia associated with haemoglobin Q rather than with haemoglobin A as in the cases hitherto described. Absence in our patient of haemoglobin F and of a raised haemoglobin A_2 fraction, both of which are often associated with thalassaemia, is not unusual in haemoglobin H-thalassaemia (Motulsky, Fessas, personal communications; and observations of the authors in Singapore and London). Nevertheless on the basis of the available evidence we prefer to call the condition haemoglobin Q–H disease.

Summary

A Chinese male patient in Singapore was suffering from a chronic hypochromic anaemia which did not respond to treatment with iron. There were unusual x-ray findings in the skeleton. The haemoglobin was composed of haemoglobin H and of another new haemoglobin which has been named haemoglobin Q. On paper electrophoresis at alkaline *p*H it moves more slowly than haemoglobin A and slightly faster than haemoglobin G. The condition has been named haemoglobin Q–H disease. The mother, who is the only member of the family available for study, has been found to be an asymptomatic carrier of haemoglobin Q.

Grateful acknowledgment is made to Dr. Lie-Injo Luan Eng, of the University of Indonesia, Djakarta, for her interest in these studies, to Dr. Tan Bock Yam, of the General Hospital, Singapore, for assistance in the investigation and care of the patient, and to Mr Ong Soong Lim for valuable technical assistance.

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HAEMOGLOBIN K IN SINGAPORE

BY

F. VELLA, M.D., B.Sc., B.A.(Oxon)

Department of Biochemistry, Faculty of Medicine, University of Malaya, Singapore

Haemoglobin K is a fast-moving haemoglobin having electrophoretic properties similar to but not identical with those of haemoglobin J. It has so far been reported in three Berber families in North Africa (Cabannes *et al.*, 1956), in a number of Liberian natives (when it was provisionally named "Liberia II") (Robinson *et al.*, 1956), in three members of the Dagomba tribe in Northern Ghana (Edington and Lehmann, 1957), and in two related East Indians resident in London (Ager and Lehmann, 1957).

Report of Two Examples

In the course of a survey of the incidence of abnormal haemoglobin by the technique of paper electrophoresis, haemoglobin K was detected, together with normal haemoglobin, in an Indian patient suffering from a psychosis, in Singapore. With the help of Dr. Gwee Ah Leng a family study was attempted, and it was found that the abnormal haemoglobin was transmitted by the mother to the propositus and to his brother. The father, who is of Indonesian–Malay origin, was carrying normal haemoglobin only. The mother is of north Indian origin and was adopted when young. The exact geographical origin of her family is indefinite. No clinical or haematological abnormality which could be attributed to the presence of the abnormal haemoglobin could be detected in any member of this family.

Another instance of haemoglobin K trait has been found in a Malay woman attending a maternity and child welfare clinic in Singapore. Her parents are pure Malay from Malacca. She is suffering from a hypochromic anaemia attributable to repeated frequent pregnancies and to worm infestation. A family study in this case has not yet proved feasible. This is the only case of haemoglobin K trait so far found in over 1,500 Malays studied.*

Blood samples from the propositus in the Indian family and from the Malay woman were compared by Dr. H. Lehmann against haemoglobins H, J, and K, and both were found to be identical with haemoglobin K.

Though the incidence of this abnormal haemoglobin appears to be very low, it seems clear that it is not restricted to any one ethnic group.

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*Since this note was submitted for publication a further case has been seen in a Malay from Penang; this brings the incidence to two out of 2,400 Malays so far studied.

MAINTENANCE OF POSTURE BY HYPNOTIC SUGGESTION IN PATIENT UNDERGOING PLASTIC SURGERY

BY

DENYS KELSEY, M.B., M.R.C.P.
Psychiatrist

AND

J. N. BARRON, F.R.C.S.Ed.
Director of Plastic Surgery, Plastic and Oral Surgical Centre, Odstock Hospital, Salisbury

A recurrent problem in plastic surgery is the maintenance in apposition of two normally widely separated areas while tissue is being transferred from one to the other. The mechanical measures usually employed, such as plaster-of-Paris, frequently immobilize most of the patient's joints and create a series of difficulties in themselves. The patient is often uncomfortable; nursing may be heavy and difficult; troublesome plaster sores may develop; whilst the stiffness that occurs in the immobilized joints may require weeks of physiotherapy for its relief.

In view of all these difficulties, when the possibility of securing fixation by means of hypnotic suggestion occurred to us a trial was made without delay upon a patient who happened to be in the ward. The patient, aged 24, had suffered an extensive loss of tissue from the fore-part of the right foot, which was to be repaired with a pedicle from the abdomen transported via the left forearm. The pedicle had already been raised and was just ready to have its upper end transferred to the forearm.

It has long been known that in certain subjects under hypnosis it is possible to place them in bizarre postures and, by appropriate suggestions, cause them to remain fixed there until the suggestion is given for their release. By the use of "post-hypnotic suggestion" it is possible to cause them to remain fixed after the hypnotic state has been terminated. There is no theoretical limit to the time that a post-hypnotic suggestion, once effective, will remain so, and by periodic reinforcements its effect could be prolonged indefinitely. A position maintained in this way is done without fatigue and without the conscious concern of the subject.

These were the techniques which we proposed to apply to the patient, and he readily agreed to co-operate. We could not have wished for a more encouraging subject.

Preliminary Procedure

At the first attempt the patient reached the deepest level of hypnosis; that is, he was able to open his eyes, talk, and move about freely whilst still remaining under hypnosis. Complete analgesia to pin-prick was soon achieved (though never, for some reason, to the cut of a scalpel). We next proceeded to the fixation of the left arm in the position against the abdomen which would be called for at and following the operation. The arm was placed in position and the patient was told that, at the command "Lock it," the arm would become fixed in that position and would not move from it under any circumstances until the command "Unlock it" was given. The result was successful. He could not move it voluntarily, nor could two attendants, using considerable vigour, pull it away. After this test the command to unlock it was given. Next it was suggested to him that on future occasions when certain specified persons said to him, "Now I am going to send you to sleep," and then counted from 1 to 10, he would pass into a hypnotic state exactly of the same depth as he had achieved that day. He was then awakened and went back to the ward.

A few days later the second session was held. It was exactly similar to the first, except that hypnosis was satisfactorily induced by using the formula suggested at the first session.

After a further few days a third session was held. On this occasion, however, the arm was not released after fixation. Instead, he was told that it would remain in position overnight while he slept. This, we felt, was a crucial point. We were delighted to find next day that he had slept well and that the position of the arm had not changed at all. It was now thought to be justifiable to perform the operation.

Operation

The patient was brought to the theatre without premedication, and hypnosis was induced in the usual manner. It was hoped that it might be possible to perform the operation under hypno-analgesia alone, but, though he was completely anaesthetic to pin-prick, he expressed some discomfort at the incision by a scalpel. Some local analgesic was therefore injected. The upper end of the pedicle was freed from the abdomen and inserted into the left wrist. A light dressing was applied and the forearm and wrist were adjusted to the optimal position. He was then ordered to lock it. Suggestions of freedom from any post-operative discomfort were given, and he was brought out of hypnosis and returned to the ward.

The position was maintained accurately until released at the next operation, three weeks later, when the lower end of the pedicle was also freed from the abdomen and inserted into the forearm. It was observed with astonishment that, from the moment of release, movement at the elbow and shoulder was completely normal—full, free, and painless.

In due course the pedicle was ready for one end to be freed from the wrist and inserted into the fore-part of the right foot. A day or two before the operation a rehearsal session was held. Hypnosis was induced and the patient's left hand was then placed on the dorsum of the right foot. He was commanded to lock it there, and told that he would maintain the position throughout the night's sleep until the morrow. Again the result was all that could be desired, and two days later the operation was performed.

The patient was again placed under hypnosis, and suggestions of analgesia were given. They were supplemented with careful injections of local analgesic into both the hand and the foot. Perfect analgesia resulted, which cannot always be obtained in the foot despite every care. When the moment came for the insertion of the freed end of the pedicle into the prepared site on the foot the convenience of having a fully co-operative patient, in contrast to the problem met under a general anaesthetic, was greatly appreciated.

The insertion was accomplished uneventfully and a light dressing was applied. The left forearm was then placed in the precise position required on the dorsum of the right foot and the patient was commanded to lock it. It was then emphasized to him that movement in all other joints would be limited only by the proviso that the position of the left forearm in relation to the right foot would remain constant. It was further stressed that there would be no post-operative discomfort of any kind and that he would sleep normally. Hypnosis was then terminated and he returned to the ward.

Actually the patient required small doses of sedative on each of the first three nights to assist him to sleep sitting up. In all other respects the suggestions were completely effective. By appropriate combinations of flexion of spine and hip with extensions of knee and elbow, and vice versa, he achieved truly astonishing mobility. He was able to feed himself and attend to all his own hygiene and toilet, even

to the extent of taking a bath. He could move about freely with the aid of one crutch and sit comfortably in a chair. Morale remained high throughout. There was never the slightest apparent shift of the forearm and hand on the foot.

Waking and sleeping, this state of affairs was maintained until, after 28 days, the pedicle was deemed fit for complete separation from the forearm. He was then hypnotized, the attachment of the pedicle to the wrist was severed, and the suggestion given to "unlock." Immediate testing revealed free and full movement at every joint, large and small. The spine could be hyperextended; the fingers of the left hand could manipulate a cigarette lighter. A totally unexpected and most agreeable finding was completely normal skin without a trace of maceration at the surfaces of the left hand and right foot, which had been in apposition.

Discussion

The benefits of this form of fixation in this case were self-evident. It cannot, of course, be expected that every case would respond likewise, but the presence of one such successful case in the ward might be expected to predispose new arrivals favourably. The induction of hypnosis is not difficult to learn, though for reasons which are far from clear some operators tend to be more consistently successful than others. Once one member of a hospital staff began to acquire some reputation in this respect his percentage of successes would be likely to increase.

The initial induction of hypnosis may take upwards of half an hour. Once this has been achieved, however, appropriate suggestion will enable any specified person to re-induce that state in a few moments and carry out the further preparation of the patient. There is no reason why, for example, members of the nursing staff or physiotherapists should not be trained in this part of the work. This would have the advantage that the patient and staff, after the initial induction, are rendered independent of the hypnotist, who is also in no way tied.

From the surgical point of view it was feared that the muscular contraction involved in maintaining the position might cause venous stasis to the detriment of the pedicle. In the event there was no evidence to suggest that this was the case.

Psychologically, it was interesting that the suggestions remained effective throughout normal sleep. Would they remain so under a dose of thiopentone? If the patient were to stumble, might he then reflexly try to wrench his hand free to save himself? One feels that investigation into these points might clarify the relationship between that altered state of consciousness we call hypnosis on the one hand and that produced by a sub-anaesthetic dose of thiopentone and by states of hysterical dissociation on the other.

It is felt that hypnosis, when possible, could provide the ideal method for those patients with burns who require frequent anaesthetics for their dressings, since no meals need be missed. This is an important consideration when maintenance of the level of plasma proteins is a difficulty.

Summary

A case is described in which the fixation of the left hand in apposition to the right foot, for the purpose of transferring tissue, was achieved by hypnotic suggestion. The technique is described in detail, and the advantages of the method and the possibilities of its wider application are discussed. Attention is drawn to points of psychological interest.

We should like to record our appreciation to our patient for his readiness to co-operate in the experiment, which might, almost too literally, have come unstuck, to his very considerable disadvantage.

Medical Memoranda

Massive Doses of Bemegride and Amiphenazole in Treatment of Barbiturate Poisoning

The value of bemegride and amiphenazole in the treatment of barbiturate poisoning has been fully established since their introduction by Shaw *et al.* (1954) and Shulman *et al.* (1955). Untoward effects from these drugs are rare, but in excessive dosage vomiting, convulsions, and psychic disturbances have been reported.

In the following case exceptionally large doses of both drugs were used without mishap.

CASE REPORT

A spinster aged 58 was seen in the casualty department of the Luton and Dunstable Hospital on October 27, 1956, at 3.15 p.m., having taken a large overdosage of butobarbitone ("soneryl") tablets approximately 17 hours before admission. The actual amount taken was never established. She was deeply unconscious, the pulse was feeble, rate 64 a minute, blood pressure 80/60 mm. Hg, respirations 20 a minute. There were moist sounds in the chest. The pupils reacted to light, but the corneal reflexes and the reflexes of the arms and abdomen were absent. The knee-jerks were present, but the ankle-jerks and plantar reflexes were absent; there was no response to painful stimuli. Treatment was started immediately; the stomach was washed out, a 5% dextrose–saline drip infusion was set up, and at 4.15 p.m. crystalline penicillin, 500,000 units six-hourly, was started. Bemegride and amiphenazole treatment was then begun, 1 ml. (15 mg.) of amiphenazole, followed immediately by 10 ml. (50 mg.) of bemegride, being injected every three to five minutes into the rubber tubing of the drip. At 5.55 p.m. the "safe state" had been reached, indicated by the return of muscle tone and all reflexes, after a total dose of 1.1 g. of bemegride and 0.33 g. of amiphenazole had been given. The blood pressure was then 100/50 mm. Hg, pulse 90, and respirations 25; all reflexes were present. The patient made some attempts at retching and responded to painful stimuli. Treatment was discontinued. At 11.50 p.m. the signs were unchanged.

At 9 a.m. on October 28 the signs were the same. At 3.30 p.m. no reflexes were present and the patient did not respond to painful stimuli. As there had been no improvement by 6 p.m., bemegride and amiphenazole treatment was restarted, the injections being given at approximately five-minute intervals. A further 5 g. of the bemegride and 1.5 g. of amiphenazole were necessary before the "safe state" was again reached by 3 a.m. on October 29. Blood pressure was 120/60 mm. Hg, and pulse 100; all reflexes were again present, the patient reacted to painful stimuli and attempted to retch. At 3.30 p.m. the signs were the same and she seemed to be more conscious. Lumbar puncture at this time showed the C.S.F. was clear and colourless; pressure 170 mm. water.

At 9.30 a.m. on October 30 the patient was still unconscious and, apart from a corneal reflex, no other reflexes could be obtained. There was no response to painful stimuli; the temperature was 102° F. (38.9° C.); she was flushed, sweating, and slightly cyanosed; the respiratory rate was 30, and there were moist sounds all over the chest.

Her condition had greatly deteriorated, and, although she had had large doses of bemegride and amiphenazole, it was felt that unless she was brought to the "safe state" fairly rapidly she would succumb from her bronchopneumonia. It was therefore decided to restart bemegride and amiphenazole treatment. A further dose of 7.9 g. of bemegride and 2.37 g. of amiphenazole was necessary before the "safe state" was again reached. She began voluntary movements of her arms and legs soon after a response had been

obtained, and four hours later was conscious enough to follow moving objects with her eyes.

She began speaking on October 31; her condition continued to improve, and she was transferred to the Three Counties Hospital, Arlesey, 11 days after admission, as a voluntary patient.

COMMENT

This patient was treated with massive doses of bemegride and amiphenazole. Within four days the total dose of bemegride was 14 g. and of amiphenazole 4.2 g. No toxic effects or side-effects were noted. The previous highest dose reported was 6.95 g. of bemegride and 2.08 g. of amiphenazole (Clemmesen, 1956). It is interesting that the only psychic disturbance of those reported by Kjaer-Larsen (1956) was amnesia regarding the attempted suicide. Dr. R. J. Russell, assistant psychiatrist, reports: "This woman appeared to be a straightforward case of melancholia, and she has responded to E.C.T. in the normal manner. Bemegride and amiphenazole treatment had no deleterious effect on her mental state."

I thank Dr. Thomas Parkinson for permission to publish this case and for his helpful criticism and advice.

G. W. MEARS, M.B., B.S.,
Late Senior House Officer, Luton and Dunstable Hospital.

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Oxygen for Foetal Distress in Domiciliary Midwifery

The following case report may suggest the practicability of oxygen therapy for foetal distress in domiciliary midwifery.

CASE REPORT

The patient, aged 45, had had four previous pregnancies. The first (1935) ended in the stillbirth of a 10-lb. (4.5-kg.) post-mature baby. The second pregnancy (1936) was terminated by surgical induction, with normal delivery of a 7½-lb. (3.4-kg.) baby; the placenta had to be removed manually. Surgical induction for post-maturity was again performed at the third confinement (1941), and a 7½-lb. (3.4-kg.) infant was delivered. The fourth pregnancy (1950) was normal. The child weighed 7 lb. 5 oz. (3.3 kg.).

In the present pregnancy labour began at 7 a.m. on November 14, 1956, with a slight show and intermittent backache. The head was well engaged and the foetal heart was noted to be well on the right side. At 2 p.m. the patient was given castor oil, 2 oz. (57 ml.), a hot bath, and an enema. Irregular pains continued, causing little distress, and she slept for two hours during the night. At 8.15 a.m. the following day the membranes ruptured. The liquor was very thick with meconium—so much so that the attendant midwife was convinced the patient was passing faeces per vaginam. Contractions became regular every 10 minutes. When seen by one of us at 11 a.m. the maternal condition was good, the cervix three-quarters dilated, and the foetal heart 120 a minute. At noon the foetal heart became irregular at 120–130 a minute. A frequent rhythm was two beats followed by a pause. Oxygen therapy was begun, using an intermittent-flow apparatus, the patient inhaling during contractions and then for a further half a minute. Absorption of oxygen was evident from the patient's colour. After half an hour vaginal examination revealed an anterior lip of cervix only. Contractions were fair, one every five minutes, and the foetal heart was unchanged. At 1.30 p.m. the foetal heart was less easily heard and had slowed to 100–110 a minute. The irregularity persisted. Contractions were stronger. The maternal condition, probably in part owing to the inhalation of oxygen, was very good (pulse 90 a minute). The patient was then examined vaginally by both of us. There was still an anterior lip of cervix, but it was agreed to carry out a forceps delivery.

An electric fire was extinguished and the patient anaesthetized without difficulty by ether alone in the left lateral position. Forceps were applied and slow extraction was performed during contractions. The head was delivered face to pubes (2 p.m.). On delivery the child (a male) was limp but blue, and soon took gasps. Regular respiration was established in a few minutes. A second-degree tear was sutured. Ergometrine, 0.5 mg., was given intravenously with delivery of the shoulders, and the uterus contracted well. Separation of the placenta had not occurred 20 minutes after delivery, and so, after Credé's method had been tried once without success, with the patient still on her side, the placenta was manually removed. Blood loss was minimal. The patient's condition remained excellent and the infusion of plasma substitutes, although these were available, was not indicated. While she was still anaesthetized further ergometrine, 0.5 mg., and prophylactic penicillin and streptomycin were given by intramuscular injection. The secundinae were deeply meconium-stained. The placenta was otherwise normal, but the cord was of excessive length and contained a true knot.

COMMENT

The successful outcome of this labour is of interest in view of the long period of foetal distress (4¼ hours). FitzGerald and McFarlane (1955) showed that where frank meconium was passed 69% of foetuses were stillborn or in a poor or fair condition. The figure for a slow heart rate was 56% and for irregular rhythm 59%. All these signs were noted in our case, and we presume the foetus was exposed to considerable hazard. In the event the child's condition was not characteristic of white asphyxia, since, although toneless, it yet had the blue colour associated with normal recent delivery and respiration was soon established. We think it likely that oxygen therapy played some part in maintaining the condition of the foetus.

Oxygen therapy was given by a portable apparatus usually employed for dental anaesthesia and capable of delivering pure oxygen, but a Minnitt apparatus could probably be used with benefit to enrich the atmospheric oxygen.

The causes of the distress can be apportioned between prolonged labour due to occipito-posterior presentation, constriction of placental site after rupture of the membranes, especially during contractions, post-maturity, and the knot in the cord.

In further reference to the article by FitzGerald and McFarlane we would support, as an additional sign suggesting increasing distress, progressive diminution of loudness of the foetal heart when the hearing conditions, point of auscultation, and listener are unchanged. The sign may be of importance on those few occasions when it is advisable to give oxygen therapy while full dilatation of the cervix is awaited. Its recognition is an indication for immediate delivery if possible.

In parenthesis, we hold that the left lateral position, which avoids the danger of vomit inhalation, is the logical and practical position for vaginal operations in midwifery. The anaesthetist is relieved from anxiety and the major present-day risk of the operation is eliminated.

Finally, it was felt that success with this case was also partly attributable to consideration of the psychological aspect of the confinement. An attempt was made not to be too rigidly bound by medical indications for hospital confinement. We accept the modern view that acceding to a patient's wishes whenever possible exerts a favourable influence upon the course of labour. The patient's co-operation throughout a long labour was excellent. The puerperium was uneventful. For the first time the patient was able to breast-feed.

T. B. L. BRYAN, M.D.
W. G. DAWSON, M.B., D.A., D.Obst.R.C.O.G.
General Practitioners.

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Reviews

TRAQUAIR'S PERIMETRY

Traquair's Clinical Perimetry. Seventh edition, by G. I. Scott, M.A., M.B., F.R.C.S.Ed. Foreword by Norman M. Dott, C.B.E., M.B., F.R.C.S.Ed. (Pp. 333+xv; illustrated. 60s.) London: Henry Kimpton. 1957.

In 1920 Traquair won the Middlemore Prize for his essay on "Perimetry: Its Method and its Value to the Ophthalmic Surgeon." This work was amplified, and in 1927 *An Introduction to Clinical Perimetry* made its appearance in the form of a textbook emphasizing the simple basic principles of technique and the clinical interpretation of the findings. Quantitative perimetry of the visual field, initiated by Bjerrum around the turn of the century, was exploited first by Roenne and later by Traquair, who added more and more to his textbook with time, so that the later editions contained a vast amount of information. The tyro turning its pages for the first time was weighed down by its sheer thoroughness. The seventh edition has been edited by Professor G. I. Scott, who has seen the need for simplification and has wisely taken advantage of this opportunity. A fuller discussion of the applied anatomy of the visual pathway forms the basis of his teaching, and on this foundation has been built the complicated edifice of the visual field in disease.

Ophthalmologists everywhere owe a great debt to Traquair, and in a sense we are all his pupils. Professor Dott in his foreword has made it plain that the ophthalmologist is not the sole legatee, but the neurologist is also a grateful beneficiary. This is borne out in the distribution of the text, in that affections confined to the choroid and retina occupy some 50 pages, whereas 140 pages are devoted to chapters on lesions of the optic nerve, chiasma, and suprachiasmal pathways. Even the white- or red-headed hatpin, the hallmark of the neurologist, is not overlooked, and his favourite test, by confrontation, is adequately described and its value when properly performed duly recognized. The advances in knowledge in optic neuropathy and on affections of the anterior part of the optic radiations are fully described, and notes are included on changes in the visual fields in thyrotropic exophthalmos and following the operation of mitral valvulotomy.

This is the first edition posthumous to its original author, and its new title *Traquair's Clinical Perimetry*, together with a short biographical sketch and photograph of the late H. M. Traquair, forms a fitting tribute from the new editor to the memory of a forthright teacher and an industrious clinical observer. The work is in safe hands and will undoubtedly retain the highest place in medical literature.

STEPHEN MILLER.

MEDICAL TREATMENT

Medical Treatment. By Kenneth MacLean, M.A., M.D., F.R.C.P. With Chapters on the Tropical Diseases by Colonel W. R. M. Drew, C.B.E., F.R.C.P., D.T.M.&H. (Pp. 696+vii. 50s.) London: J. and A. Churchill Ltd. 1957.

This book is written in the belief that in many of the standard textbooks of medicine the sections on treatment have not received the increasing attention which they deserve. It follows the pattern of these textbooks, beginning with diseases of the heart and blood vessels and progressing steadily through the various systems. Aetiology and description of the disease to be treated are cut to a minimum, and, though inevitably a good deal is included which is not strictly treatment, the author has avoided the pitfall of writing a textbook of medicine. The three final chapters deal with "Fluid and Electrolyte Disturbances"; "A.C.T.H., Cortisone and Allied Steroids"; and "Antibiotics and Sulphonamides." The index is the backbone of a book of this kind, and this one is excellent. The book will be of most value to the student and the houseman, as it gives a clear-cut outline of rational treatment for all the diseases they are likely to meet. Of course it is always easy to disagree on details, and I personally do not regard "myleran" as the treatment of choice in chronic myeloid leukaemia, and in ulcerative colitis I prefer "salazopyrin" to the sulphonamides mentioned by Dr. MacLean. In general, however, one can only praise Dr. MacLean's balanced modernity. The faults are those which are inherent in a book of this kind. Its very comprehensiveness means that a number of topics are dealt with so briefly as to be hardly worth the mention. For reasons of space, possibly, the outlook is somewhat mechanistic, and there is a lack of emphasis on what we call general management and the Americans call total patient care. The experienced doctor who wants help in treatment will not find this book as helpful as the American annual publication, *Current Therapy*, of which the 1957 volume was reviewed here a few months ago, but perhaps this is merely to repeat that this is primarily a textbook for students.

L. J. WITTS.

ATLAS OF DERMATOLOGY

An Atlas of the Commoner Skin Diseases. By Henry C. G. Semon, M.A., D.M., F.R.C.P., revised with the collaboration of Harold T. H. Wilson, M.A., M.D., M.R.C.P., D.T.M. Colour photography originally directed by the late Arnold Moritz, B.A., M.B., B.C. Fifth edition. (Pp. 375+viii; 153 colour plates. £5 5s.) Bristol: John Wright and Sons Ltd. 1957.

Dermatological diagnosis is in large part visual, and for those who are not expert in skin diseases an atlas may be of the greatest value. Although at first sight five guineas may seem a good price to pay for a text of elementary dermatology, a moment's reflexion enables us to recall that 153 full colour plates for this price is very cheap. Presumably it is possible only because many of the plates from the four previous editions are preserved, but nevertheless a number of good fresh ones have been added. There are, it is true, a few plates that fall below the general standard, but this atlas remains, in its size, scope, and achievement, the only one of its kind in the English language. Language is relevant because at least an equal space is taken up by the written text. This, originally by Dr. Semon, has been revised in the present edition with the collaboration of Dr. Wilson. In most of the text the style of the senior author is preserved, and, although the book has been brought up to date, one can feel that the old "Semon" is still there. It is, of course, inevitable that a text of this sort has to be selective and cannot aim at completeness, but, although modern ideas and treatment (mostly up to the early 1950's) are incorporated, there still remains room for the more empirical methods which they have, perhaps only temporarily, replaced. There is no doubt that this atlas will continue to fulfil a demand and prove invaluable to the busy practitioner.

F. R. BETTLEY.

CLINICAL ORTHOPAEDICS

Clinical Orthopaedics—No. 9. Editor-in-Chief: Anthony F. DePalma. With the assistance of the Associate Editors, the Board of Advisory Editors, and the Board of Corresponding Editors. (Pp. 353+xii; illustrated. Single copies 60s.; subscription price 48s.) Philadelphia and Montreal: J. B. Lippincott Company. London: Pitman Medical Publishing Co. Ltd. 1957.

The contents of the three sections of the ninth volume are the pathological physiology of metabolic bone disorders, general orthopaedics, and motorist injuries and motorist safety. The editor of the first section has collected a team of writers from New York, Washington, Baltimore, Chicago, and Iowa. In this symposium there is no attempt to cover the whole subject, but the earlier chapters provide a good contribution to our knowledge of the physiology and histology of bone. A highly technical report of the theories of bone mineral structure with information on crystal structure and bone apatite is followed by a study of the organic

matrix of bone and epiphysial cartilage. The most attractive chapters on the disorders are one by a radiologist on affections characterized by osteosclerosis, and the other by Snapper, which is a masterly review of the present knowledge of multiple myeloma. In a fascinating manner he describes how this has been pieced together, and the importance of laboratory findings before making a diagnosis. The chapter on human and rat lathyrism is not convincing, particularly as the two appear to be different diseases.

In the general section a largely pictorial article on skin grafts in hand surgery includes general principles of the subject as well as the practical aspect. The reader is likely to be interested in the management of idiopathic scoliosis. This difficult subject has been attracting the attention of surgeons in many countries, and John H. Moe (Minnesota) writes with experience. He knows of the work of J. I. P. James in this country and pays tribute to Cobb, Schmidt, and others, and gives his own views on determination of treatment with the "how, where, and when to correct and fuse," ending with causation of the failures. The articles on motor safety and prevention of accidents are of a type not found in the medical journals published in this country. They include information on driver proficiency, methods of testing drivers, safety belts, and motor-vehicle design, and contain a mixture of administrative, engineering, and medical problems. As in the previous volumes, the illustrations are of a high standard and well chosen.

ST. J. D. BUXTON.

THE FOREQUARTER AMPUTATION

The Forequarter Amputation. By H. F. Moseley, M.A., D.M., M.Ch.(Oxon), F.R.C.S.(Eng. and Canada), F.A.C.S. Illustrated by Helen T. MacArthur, B.A. (Pp. 79+viii; illustrated. 42s.) Edinburgh and London: E. and S. Livingstone, Ltd.

Berger wrote the first detailed account of the "forequarter" amputation in 1887, though it is here mentioned that the operation had been performed as early as 1808 by Ralph Cuming. The operation is seldom required, yet it may fall to the lot of any surgeon to have to perform it, and this beautifully produced and well-illustrated monograph should prove of great service in facilitating its performance. Both the anterior and the posterior (Littlewood's) approaches are described and illustrative cases are provided. A special chapter gives an account of all the 68 recorded "traumatic forequarter amputations." These make astounding reading. Most of them resulted from the arm being caught in machinery, and in several of the cases complete avulsion of the arm was followed by very little bleeding. Belchier recorded such a case in 1737, and Cheselden included a picture of the patient in his book on the *Anatomy of the Human Body*.

The present book fills a need, but there is still greater need for a monograph on the "hindquarter" amputation. I trust that we shall in due course have such a companion volume from the pen of that great British surgeon (Sir Gordon Gordon-Taylor) who has had a unique experience of the inter-innomino-abdominal amputation.

ZACHARY COPE.

CEREBRAL LIPIDOSES

Cerebral Lipidoses: A Symposium. Chairman: L. Van Bogaert, M.D.; Editor: J. N. Cumings, M.D., F.R.C.P.; Associate Editor: A. Lowenthal, M.D. (Pp. 212+x; illustrated. 42s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1957.

The pathology of the rare group of lipid-storage diseases and leucodystrophies has long remained obscure, but the recent application of new histochemical methods and improved analytical techniques has given valuable new information about the chemical nature of the lipid deposits, and there are signs that order is at last beginning to emerge from chaos in this field. If there are any regrets at the passing of the colourful old names—Tay–Sachs's disease, Neimann–Pick's disease, Hand–Schüller–Christian's syndrome, and morbus Gaucher—it is a compensation that the new chemopathological terms "gangliosidosis," "sphingomyelinosis," "cholesterolosis," and "cerebrosidosis" are more meaningful and more precise. The new names remind us also of the possibility that some of these diseases may belong to the group of conditions in which inborn metabolic errors are caused by the failure of specific gene-controlled enzymes. The significance of this work is clearly not limited to the few rare conditions hitherto described, for the concept of organic dysfunction due to biochemical lesions involving enzymic imbalance may well be applicable in a considerably wider group of conditions.

This book gives the proceedings of a symposium organized by the Inter-University Foundation of Neuropathological Research and held at Antwerp in July, 1955. The participants were mainly interested pathologists and biochemists, and the general standard is as high as may be expected of contributions coming from leading authorities such as Blackwood, Brante, Chatagnon, Cumings, Diezel, Edgar, Froehlich, Klenk, Pearse, Seitelberger, and Svennerholm. Besides the better-known storage diseases of the textbooks, this book contains chapters on still rarer conditions, such as the "cephalin-lipidosis" of Baar and the "lipo-glyco-protidic thesaurismosis" described by Seitelberger. The last chapter, by H. Debuch, is on the chemistry of the acetalphosphatides. It may be noted that these compounds are now known to be $\alpha\beta$-unsaturated ethers, so that parts of this chapter now need to be revised. The book is admirably produced, with a large number of colour plates, and it can be recommended highly to anyone wishing to learn more about recent advances in this field.

DEREK RICHTER.

IMPAIRED FERTILITY

From Sterility to Fertility. A Guide to the Causes and Cure of Childlessness. By Elliot E. Philipp, M.A., M.B., B.Chir., F.R.C.S., M.R.C.O.G. (Pp. 120; illustrated. 10s. 6d.) London: Thorsons Publishers Ltd. 1957.

"Most readers of this book will be married couples who are themselves suffering from infertility. . . ." It is primarily designed for such, and therefore consists of a simple account of sex anatomy and physiology, and of the causes, investigations, and treatment of impaired fertility. It aims to ensure intelligent and willing co-operation between the infertile couple and their medical attendant, saving the latter the need for much explanation. Mr. Philipp perhaps over-emphasizes the good which can accrue from the investigation and treatment of sterility, and understates the value of time, chance, and opportunity. His undue optimism over the results of tubal reconstruction operations may also raise false hopes in those women who suffer tubal obstruction. Nevertheless, the information given is generally both accurate and sensible. The sections devoted to male impotence, to coital errors, to artificial insemination, and to adoption call for special mention; these alone will undoubtedly answer many of the questions which occur to afflicted couples.

Whether it is desirable for the doctor in charge of a case to be spared personal explanation could be disputed, as could the wisdom of concentrating a couple's attention on their problem by giving them a book to read. It has to be recognized, however, that some points do not always occur to either doctor or patient during discussion, and their importance may become manifest only when the sterile couple read of them in a book such as this. For its kind it has much to commend it—not least the correction of false impressions which the laity now often obtain from less authoritative writings.

T. N. A. JEFFCOATE.

The ninth edition of H. H. Clay's *Public Health Inspector's Handbook* is now available from H. K. Lewis and Co. Ltd., 136, Gower Street, London, W.C.1 (pp. xx+614; 40s.). Since the last edition the designation of "sanitary inspector" has been changed to the more appropriate "public health inspector." The book has served as a standard manual for both for the past 25 years, providing information on all aspects of training and practice.

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GOUT

The development of our knowledge of gout appears to have passed through three distinct phases. The first begins in antiquity, of which a memorial remains to this day in the form of the well-known aphorisms of Hippocrates.[1] The second, which might be called the literary phase, begins in the seventeenth century with the classical account by Sydenham[2] in 1683, to be followed by the giants of the nineteenth century, Scudamore,[3] Trousseau,[4] Charcot,[5] and many others. The third phase began in 1848, when A. B. Garrod[6] left some serum from a patient with gout on the mantelpiece overnight and noticed in the morning that a thread which he had placed in it was encrusted with crystals; he identified these as sodium urate. This observation ushered in the biochemical era, and the development of adequate biochemical methods for the accurate measurement of urate concentration in body fluids engaged the attention of biochemists for a great part of it.

Soon it became clear that the relationship between acute gout and uric acid was less simple than expected. B. M. Jacobson[7] and R. M. Mason[8] could find no regular or striking change in serum levels associated with acute attacks of gout. Familial studies on the relatives of gouty subjects[9–12] revealed many individuals suffering from hyperuricaemia who remained entirely asymptomatic. The intravenous injection of uric acid producing blood levels of over 20 mg. per 100 ml. did not precipitate attacks of gout.[13] The observation that uricosuric agents, such as probenecid, which may bring the level of uric acid in the serum to well below normal levels, actually precipitate attacks of acute gout,[14–16] together with the fact that colchicine, so specific in its effects on acute gout, has no effect on urate levels in the serum, led to the suggestion that a precursor of uric acid might be responsible for acute gout. Doubt still exists whether deposition of urate crystals precedes or follows acute attacks in the inflamed synovial tissue. L. Sokoloff[17] has found crystals in biopsy material while others[18] have claimed that no urate crystals were present in biopsy material from a first attack of gout. The alternative hypothesis first put forward by S. J. Thannhauser,[19] and still maintained by him,[20] that the primary defect lies in the kidney, consisting of an excessive resorption of urate by the tubules, has received little support and has, indeed, been vigorously attacked.[21] Tracer studies with radioactive isotopes now bid fair to pinpoint the metabolic defect of gout as an abnormality of purine metabolism. When glycine labelled with nitrogen-15 is injected into gouty subjects, the incorporation of nitrogen-15 into urinary uric acid is greater and faster than normal.[22] This phenomenon could be detected only in some 25% of gouty subjects—a curious finding which pointed to the conclusion merely that in at least some gouty subjects there was over-production of uric acid. J. B. Wyngaarden[23] and his colleagues, of the National Institute of Arthritis and Metabolic Diseases at Bethesda, U.S.A., have recently been able to use glycine labelled with carbon-14; this has enabled them to give more nearly physiological doses, and they have shown that all gouty subjects produce excess uric acid. In addition they have been able to label 4-amino-5-imidazolecarboxamide (A.I.C.)[24 25]—that is, to label a substance entering the metabolic pathway after glycine. Again they found that this was more rapidly incorporated into urinary uric acid in all gouty subjects. In addition, administration of A.I.C. reduced the appearance of ^{15}N-labelled glycine, given simultaneously, in the urine, but not in creatinine, of which glycine is also a precursor.[26] This suggests there may be a control mechanism for purine metabolism. Indeed, this effect was less noticeable in gouty subjects, so it is possible that a defect in this control mechanism is part of the metabolic disorder of gout. From other data these workers suspect that a derivative of guanilic acid, 8-hydroxy-7-methylguanine, may play some part, and there is evidence

[1] Hippocrates, *The Genuine Works of Hippocrates*, 1849, trans. by Francis Adams, London, Sydenham Society.
[2] Sydenham, T., *The Whole Works of that Excellent Practical Physician, Dr. Thomas Sydenham* 1722, trans. by John Pechey, London.
[3] Scudamore, C., *A Treatise on the Nature and Cure of Gout and Gravel*, 18 3, London.
[4] Trousseau, A., *Lectures on Clinical Medicine at the Hotel-Dieu, Paris*, 1865, trans. by J. R. Cormack, London, New Sydenham Society.
[5] Charcot, J. M., *Clinical Lectures on Senile and Chronic Diseases*, 1881, trans. by William S. Tuke, London, New Sydenham Society.
[6] Garrod, A. B., *Med.-chir. Trans.*, 1848, **31**, 83.
[7] Jacobson, B. M., *Ann. intern. Med.*, 1938, **11**, 1277.
[8] Mason, R. M., *Proc. roy. Soc. Med.*, 1951, **44**, 289.
[9] Talbott, J. H., and Coombs, F. S., *J. clin. Invest.*, 1938, **17**, 508.
[10] Smyth, C. J., Cotterman, C. W., and Freyberg, R. H., ibid., 1948, **27**, 749.
[11] Stecher, R. M., Hersh, A. M., and Solomon, W. M., *Ann. intern. Med.*, **31**, 595.
[12] Hauge, M., and Harvald, B., *Acta med. scand.*, 1955, **152**, 247.
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[15] Gutman, A. B., and Yü, T. F., *Advanc. intern. Med.*, 1952, **5**, 227.
[16] —— —— *Lancet*, 1957, **2**, 1258.
[17] Sokoloff, L., *Metabolism*, 1957, **6**, 230.
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[19] Thannhauser, S. J., *Lehrbuch des Stoffwechsels und der Stoffwechselkrankheiten*, 1929, Munich.
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[21] Stetten, De W., Talbott, J. H., Seegmiller, J. E., Wyngaarden, J. B., and Laster, L., ibid., 1957, **6**, 88.
[22] Benedict, J. D. Roche, M., Yü, T. F., Bien, E. J., Gutman, A. B., and Stetten, De W., ibid., 1952, **1**, 3.
[23] Wyngaarden, J. B., ibid., 1957, **6**, 244.
[24] Seegmiller, J. E., Laster, L., Stetten, De W., *J. biol. Chem.*, 1955, **216**, 653.
[25] —— *Amer. J. Med.*, 1957, **22**, 816.
[26] —— Laster, L., and Stetten, De W., *9th International Congress of Rheumatic Diseases*, 1957, Toronto.
[27] Dent, C. E., *Amer. J. Med.*, 1957, **22**, 671.
[28] Combined Staff Clinic, ibid., 1957, **22**, 807.

that this substance is present in the urine in increased amounts during acute gout. Secondary gout, such as occurs in polycythaemia and leukaemia, may not be due necessarily to the same defect, the one being an inborn error of metabolism, the other due, perhaps, to excessive production of some metabolite which may not be identical. C. E. Dent[27] has suggested that when a hereditary metabolic disorder presents a confusing biochemical picture it is because "we have not as yet gotten down to the basic chemical pathology but are merely fiddling around with a less important secondary phenomenon."

Perhaps we have now entered the final phase—the study of intermediate purine metabolism—that is, the precursors of uric acid. The technique is made possible by the development of radioactive labels, and we may expect to solve fairly soon the fascinating problem of gout. Clinically, uric acid remains important, being responsible not only for the production of chronic arthritis but sometimes of renal disease as well. A complete understanding of the metabolic error giving rise to this disease will probably come from the U.S.A., and it is a sobering thought that a recent review of this ancient disease in the *American Journal of Medicine*[28] gives 36 references only one of which is to the British or European literature on this subject, and that is to Garrod's original observation.

SYNTHETIC HORMONES AND MEAT PRODUCTION

The discovery[1] of the oestrogenic action of one of the stilbenes, diethylstilboestrol, in 1938 led to the study of other synthetic oestrogens. Their ability to induce caponization after implantation in cockerels is one measure of this activity. The effect on the male bird of diethylstilboestrol and of hormones with a similar action is to suppress the secondary sex characteristics, with the result that these birds fatten more readily than the untreated. Their flesh is whiter and more tender, fat is deposited within the flesh, and the dressed bird is, in general, regarded with more favour as an article of food. The female bird is less sensitive to treatment with the hormone. After the application of diethylstilboestrol to poultry had proved commercially successful in the U.S.A., its effects on castrated cattle and sheep began to be studied. The results of implantation, and also of giving the compound daily in the feed,[2] showed that economic gains in meat production were possible: the conversion of feeding-stuffs into meat was more efficient in the treated animals—which is to a farmer what lowering manufacturing costs is to an industrialist. The technique has been widely adopted in the U.S.A. since November, 1954, diethylstilboestrol and oestradiol being the synthetic oestrogens mainly used to treat some two-thirds of all fattening cattle. Many millions of tons of meat and poultry have been derived from animals treated in this way. Improved conversion of feeding-stuffs into meat has also been reported after androgen–oestrogen implants (testosterone + diethylstilboestrol).

In Britain hexoestrol has been widely used for caponization of cockerels, and castrated cattle and sheep have also been treated with it. Hexoestrol has been the preferred compound, since so far as humans are concerned its potency is only about one-tenth that of stilboestrol. The effect of synthetic oestrogens on castrated cattle and sheep, whether implanted or given daily by mouth, differs from that on poultry in that more protein, more bone, and less fat are deposited.[3,4] Only a small amount of the hormone fed is absorbed, some 60% passing out in the faeces. In order to prevent remnants of unabsorbed pellets being eaten by human beings, it has been recommended that implantation should be confined to the back of the ear, and that the ear should be later destroyed. The single implanted dose of hexoestrol is about 60 mg. for cattle and 15 mg. for sheep. Given by mouth the dose is 10 mg. daily for cattle and 2 mg. daily for sheep. Farmers wishing to use this method were strongly advised to purchase a proprietary concentrate containing the oestrogen and not to attempt to mix the hormone with the concentrate themselves, since in handling the powdered material they would be in danger of absorbing harmful amounts. In the U.S.A. it has been reported that 24 mg. of diethylstilboestrol by implantation will give the same or better results than a total dose of 1,500 mg. taken by mouth.[5]

Treatment with hexoestrol offers several advantages to the farmer. The treated animals grow on an average 25% faster than the untreated; over a treatment period of 100 days bullocks will put on an extra 50 to 60 lb. (22–27 kg.) body weight, while sheep will gain an extra 8 to 10 lb. (3.6–4.5 kg.),[6] The conversion of feeding-stuffs into meat is increased by about 15–20%. The treated carcasses

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[11] Dodds, E. C., Folley, S. J., Glascock, R. F., and Lawson, W., *Biochem. J.*, 1958, **68**, 161.
[12] Briggs, G. M., *J. Amer. med. Ass.*, 1957, **164**, 1473.
[13] Hertz, R. In discussion of paper by Gassner, F. X., *et al.*, "The Effects of Hormones on Growth in Fattening and Meat Production Potential of Livestock (of Domestic Animals)," Laurentian Hormone Conference of American Association of Advancement of Science, 1957, Quebec.

contain more protein, water, and bone, and less fat than the untreated. The extra protein and water and the reduction in fat are considered by many as advantages, since the taste to-day is for lean flesh with the minimum cover of fat. This commercial "acceptability" should not be confused with quality—that is, the tenderness, flavour, and colour conventionally associated with "prime quality"—for these features are directly related to the fatness of the carcass and thus will tend to be affected adversely by hexoestrol treatment. Those customers who can afford to buy unnecessary fat for the sake of the quality of the lean meat associated with it will prefer meat from an untreated animal. But for the vast majority who want the minimum of waste fat, meat from a hexoestrol-treated animal offers a more close approach to their requirements.

The effects of this treatment on the animal are of two kinds: first, they develop the characteristics of the intact male—restlessness and riding often during the first week after implantation, greater development of the neck and shoulder, and a slight tendency for the meat to be darker in colour—then the pelvic ligaments become slack, the pelvic arch widens, and mammary development occurs. In wethers and bullocks the increase in mammary development is not important, since it is manifested only by an increase in length of rudimentary teats, but in females the udder enlarges to the point of milk secretion. Infertility, dystocia, and uterine prolapse have been observed in ewes grazing early subterranean clover of high oestrogenic content.[7] Since the amount and character of udder tissues are two of the criteria by which a grader judges a carcass, there is likelihood that carcasses from treated females will be downgraded or classified as ewes or cows and thus secure a lower price per pound. For these reasons female animals should not be treated with hexoestrol. Intact males—bulls and rams—have been treated experimentally with hexoestrol, and preliminary trials show that the effect is in some ways similar to that in poultry. They will be made temporarily sterile, but can be expected to regain fertility. It is possible, however, that their breeding ability is reduced. Treated rams do not grow faster but seem to fatten more readily than untreated, the effect being akin to surgical castration.

Extremely small doses of all closely related synthetic female sex hormones are capable of producing a physiological response in laboratory animals. The effective subcutaneous dose of *meso*-hexoestrol for the rat is 0.2 μg.[8] American work with diethylstilboestrol has shown that the amount of residual hormone in the edible meat of the treated carcasses at time of slaughter is not more that 1 part in 10 million in the sheep or chicken and usually much less; it is about one-tenth of this in beef muscle and liver. While G. S. Wiberg and N. R. Stephenson[9] found appreciable amounts of oestrogen in muscle, liver, and kidney 24 hours after the removal of stilboestrol from the diet of steers, they found none after 48 hours. So far as the effect of cooking on residual oestrogen is concerned, M. Stob and his colleagues[10] found that heating at 120–150° C. for two hours had no effect on the hormone. Men preparing the hexoestrol and also those who introduce it into the feed run the risk of receiving an overdose through an accident in the handling of the material, and this would show itself in gynaecomastia. E. C. Dodds and his colleagues[11] have recently reported that even with physiological doses the main metabolic pathway of labelled hexoestrol injected subcutaneously is rapid excretion in the urine and faeces of up to 90%, either unchanged or as an unidentified non-volatile metabolite. Less than 2% of the initial dose is totally oxidized. According to unpublished work referred to by these authors, there is no accumulation of labelled hexoestrol in muscle or in any part of the nervous system, reproductive system, pituitary gland, or mammary gland of spayed female rabbits killed 24 hours after receiving a dose of 100 μg. subcutaneously. With so large a fraction of the dose excreted so rapidly, it might be thought surprising that hexoestrol exerts so profound and persistent a physiological action as it does. But as oestrogens of the hexoestrol type are some 200 times more active when administered locally to the vagina, only a small fraction of the dose need be retained—say, in the reproductive system—to secure persistence of the response after the bulk of the dose has been excreted.

Normal foods of plant origin—such as lettuce, lucerne, clover, wheat, oats, and maize—may contain appreciable amounts of compounds of low oestrogenic activity.[12] But of greater importance is the possibility of continuous contamination of the pasturage, soil, and water with the synthetic and resistant oestrogens passed in the urine and faeces of the treated animals and the uptake of these by plants: this is over and above the contribution of natural substances spread in the manure. This accumulation of oestrogens constitutes a hazard to other stock and even directly to man,[13] though the danger will obviously be much less if treatment is given by implantation. Accidental chronic oestrogenization manifesting itself most obviously in gynaecomastia must be added to the list of possible toxic effects if the widespread use of oestrogens continues. It would seem wise to discourage their use in agriculture until more is known of the dangers, although the evidence to date indicates that, if properly administered to the animal, the consumer is unlikely to receive harm from eating the meat of treated animals.

INDUSTRIAL HEALTH SURVEY

Since 1941, when a B.M.A. committee reported on "Industrial Health in Factories," several committees of inquiry have examined the problems of organizing a comprehensive occupational health service of a national character. The latest contribution to this question—with its difficulties of finance, Governmental supervision by one or other of the three Ministries most closely concerned, and availability of doctors and nurses to maintain any such scheme—is a report[1] of a survey of industrial health in Halifax. This report is the work of H.M. Factory Inspectorate, and to each section is appended the recommendations and suggestions of the Industrial Health Advisory Committee, appointed in 1955 by the Minister of Labour and National Service to advise on the future development of industrial health services in workplaces covered by the Factories Acts. The town of Halifax was selected chiefly on account of the wide diversity of its industries and the variety of its factory buildings, many of which are of the old multi-story mill type, while many others employ only a small number of workers—557 in fact employed only 25 or under. The report describes the results of a pilot industrial health survey of 760 factories employing a total of 28,699 manual workers. It includes an examination of the structural and environmental conditions of the factory buildings, heating, ventilation, washing facilities, sanitary accommodation, canteen and meal facilities, seating, lighting, noise, possible health hazards, and first-aid, medical, and nursing services. It is quite clear from the report that in a large proportion of the smaller and older factories environmental conditions were unsatisfactory, especially heating and ventilation. The health risks, on the other hand, were less prominent in these small establishments, partly because many of them were factories only in the legal sense of the term, and included such undertakings as joiners' shops and repair workrooms of various kinds.

Industrial medical and nursing services, though accomplishing much excellent work, by no means represented an organized occupational health service. There were no full-time works medical officers and only four part-time, and no factory employed a doctor regularly for more than two hours a week. The medical examination of young persons, and of a few workers where required by special regulations, was carried out under statute by the appointed factory doctor, and of workers in silicious materials by the Pneumoconiosis Medical Panel of the Ministry of Pensions and National Insurance. There were nine full-time State-registered nurses and three State-enrolled assistant nurses employed in the factories surveyed. The provision of a comprehensive occupational health service, including medical and nursing supervision of the large number of small factories in Halifax, and in other towns with a similar industrial lay-out, would clearly present considerable difficulty. The report suggests that, in Halifax at least, general practitioners would be able and willing to undertake part-time service as works medical officers. Some have taken the view that a rapid development of medical and nursing services in industry might detract from the efficiency of the National Health Service, but the Industrial Health Advisory Committee does not think that "the speed of development is likely to be such as to produce any serious difficulties under this head for the time being."

The Halifax survey, because of the nature of the industries which it has investigated, does not emphasize the health hazards in factories where toxic dusts and vapours are an essential feature of the manufacturing processes, and the Industrial Health Advisory Committee has commented on the lack of positive information about the atmospheric concentrations of such toxins. Valuable as is the information the Halifax survey provides, it does not go very far towards solving the question whether the occupational health service of the future should be a self-contained organization, independent and centrally supervised, or an enlargement of the present system of full- and part-time works medical officers paid by the employers, appointed factory doctors and medical inspectors of factories paid by the Government, and scientific and technical advisers paid by either or both. In Halifax itself the committee recommends that the further development of medical and nursing services should "proceed by stages." Experiments designed to throw light on the wider occupational problems are being carried out in other towns such as Slough and Harlow, and the Halifax survey serves at any rate to supplement these. Many of the problems of organization and control of a national occupational health service still remain to be solved, and the belief expressed by the B.M.A. in 1954 that the time has not yet come to lay down the precise form of an occupational health service still holds good.[2]

[1] Ministry of Labour and National Service, *Industrial Health. A Survey in Halifax*, 1958. H.M.S.O., London. Price 1s. 6d. net.
[2] *British Medical Journal Supplement*, 1954, **1**, 114.

ECHO SOUNDING IN CARDIOLOGY

The measurement of intracardiac pressure and blood flow by cardiac catheterization and other techniques has greatly advanced understanding of haemodynamics and the living pathology of the heart. But flow and pressure should be related to volume changes in any system, and so far no very satisfactory way has been devised of calculating the volume changes in the heart during the cardiac cycle. The ultrasonic echo method has recently been applied to cardiological diagnosis,[1 2] and this, by affording information about the position of the walls of the cardiac chambers, may help to link volume changes with variations in pressure and flow throughout the cardiac cycle. The method depends upon the principle that at the boundary of two media ultrasonic waves are partly reflected and partly transmitted into the new medium, those waves that are reflected returning to the source as a recordable echo. The time taken for the sound to reach the new medium and return to the source is proportional to the distance of the medium from the source of sound. A vibrating quartz crystal is used to transmit ultrasonic sound waves,

[1] Keidel, W. D., *Z. Kreisl.-Forsch.*, 1950, **39**, 381.
[2] Edler, I., and Hertz, C. H., *K. fysiogr. Sällsk. Lund Förh.*, **1954**, **24**, No. 5.
[3] Effert, S., Erkens, H., and Grosse-Brockhoff, F. *Germ. med. Monthly*, 1957, **11**, 325.

and the same quartz crystal also acts as a receiver of the echo when the waves are reflected back to their source. Recently S. Effert, H. Erkens, and F. Grosse-Brockhoff[3] have used this method in the study of mitral valve disease, recording the ultrasonic echo curve of the left atrium in health and disease. They believe that the degree of mitral stenosis may be estimated from the curve. When the stenosis is severe, the passage of blood from the left atrium into the ventricle is slow and even, and inward movement of the left atrial wall during diastole is abnormally slow. With less severe degrees of stenosis more rapid inward movement is recorded. The method, however, is not confined to the measurement of the position of the outer walls of the heart, in which it would have no advantage to offer over electrokymography. Its special value lies in the fact that it enables simultaneous measurements to be made of the position of the cardiac septa and the posterior wall of the heart in addition to that of the anterior wall nearest the recording instrument. In this way it offers the possibility of arriving at an estimate of the changing volumes of the chambers of the heart throughout the cardiac cycle. A drawback to the method is the fact that ultrasonic waves of high frequency cannot easily penetrate air, so that examination of the heart can be made only over those portions of it beneath the sternum or covered at most by a thin layer of lung, but the technique appears to be safe and without discomfort to the patient.

HIGH-POTENCY CORTICOTROPHIN

The Ministry of Health has announced[1] that from April 1 the manufacture of low-potency corticotrophin will cease to be permitted under the Therapeutic Substances Act (1956). The provision of purer preparations exclusively will be widely welcomed by clinicians.

The changes to be made in the regulations under the Therapeutic Substances Act have raised formidable scientific and administrative problems, and have been based largely on the results of an international conference called by the Medical Research Council last July. The assay of corticotrophin is a rather imprecise procedure. It is much affected by the rate of utilization of the hormone, which in turn is subject to the effects of the route of administration, the degree of purity of the preparation, and the presence of such adjuvants (gelatin or others) as are added in long-acting preparations of the hormone. In all bioassays it is desirable to compare the substance under test with a standard of roughly equivalent potency and purity; in the assay of corticotrophin it is essential to do so.

The present international standard for corticotrophin is a crude preparation with a potency of 1.4 i.u./mg. (by definition). Purer preparations of corticotrophin, when assayed against the international standard, give potencies of 10–30 i.u./mg. if the assay is done intravenously, and of 30–90 i.u./mg. if the assay is done subcutaneously. This difference in potency has been called "enhancement." The enhancement factor varies from batch to batch but is usually about threefold; the reason for it is still not understood and is a subject of considerable physiological interest. The enhancement effect is also shown in man. Thus corticotrophin of high purity is relatively more effective by subcutaneous administration than by intravenous administration, as compared with a crude preparation. The possibilities for confusion in dosage, when all preparations are labelled in terms of a single unit, are thus considerable, and to overcome this confusion is the purpose of the new regulations.

The solution to the problem has been found in changing the standard preparation to be used. The World Health Organization is working on the same lines, and has started to establish a new international standard of purer material. To bridge the gap before the new international standard is ready, house standards have been created by each of the manufacturers supplying corticotrophin for the British market. Each house standard is closely similar to the material being sold by that firm, and has been carefully assayed against the existing international standard; it has had a potency assigned to it in terms of its "enhanced" activity by the subcutaneous assay. This means that, in future, all batches of corticotrophin assayed in this way will be labelled with a potency (based on subcutaneous assay in terms of the appropriate house standard) which reflects their expected potency when administered subcutaneously or intramuscularly in man. The clinician using preparations by this route need make no adjustment of dosage. The great majority of all injections of corticotrophin are nowadays given either subcutaneously or intramuscularly, and the intravenous-drip treatments are rapidly passing out of use. Consequently the changes in the regulations should cause less trouble to clinicians than they would have done formerly.

Preparations of corticotrophin intended for intravenous use will have to be labelled "For Intravenous Use Only." They will be assayed against the appropriate house standard, but by the intravenous route. Since the house standards have been assigned a potency based upon their "enhanced" subcutaneous activity, the preparations assayed against them by the intravenous route will be overvalued in potency. This overvaluation will tend to be about threefold (the mean enhancement factor), so that clinicians will find it advisable to administer intravenously roughly three times the number of units they have formerly given in order to produce the same effect. Though these changes in the regulations will cause some inconvenience, they will ultimately help to remove a major source of discrepancy in the labelling of corticotrophin and lead to a quantitatively sound basis for corticotrophin therapy.

ANNUAL MEETING AT BIRMINGHAM

In the opening pages of the *Supplement* this week we print the provisional programme of this year's Annual Meeting, to be held in Birmingham from July 10 to 18. The President-Elect is Professor A. P. Thomson, professor of therapeutics and dean of the medical school of Birmingham University. The Arrangements Committee has received unstinted help from the University, whose Great Hall, at Edgbaston, will be used for the Annual Representative Meeting. All the scientific meetings of the Sections, the Scientific Exhibition,

[1] See note at p. 781.

and the Exhibition of Pharmaceutical Products will also be held at the University. Full details of the social functions and of the meetings of the nineteen Scientific Sections are given in the provisional programme. The tendency to combine meetings of two or more Sections is again in evidence; this is popular with general audiences, for it overcomes the danger of a discussion being confined within narrow specialist limits. There should, for instance, be much to learn at the combined meeting of the Sections of Medicine, Surgery, and Gastroenterology at which "Peptic Ulcer" will be discussed. The Scientific Exhibition will house about 40 exhibits, and competition should be keen for the awards of certificates of merit for "excellence of presentation" and for "scientific merit and originality." Last year at Newcastle upon Tyne large audiences were attracted to the colour television programmes on closed circuit. During each day of the scientific meeting at Birmingham surgical operations and clinical demonstrations will be telecast in colour on a closed circuit from Queen Elizabeth Hospital, the technical arrangements being sponsored by Smith, Kline, and French Laboratories Ltd. The full and interesting programme at Birmingham is sure to attract a large number of medical visitors from Britain and overseas, and those intending to come to the Meeting would be well advised to make early application for hotel accommodation.

NEW CHAIR OF ANAESTHESIA

A gift of remarkable munificence has made possible the founding of a professorial chair of anaesthesia at the Royal College of Surgeons. Last week it was announced[1] that the British Oxygen Company has provided £150.000 to finance this professorship, which, despite Great Britain's pre-eminence in this field, is the first to be established in its capital city. A laboratory for research in anaesthesia was formally opened last year[2] (though work had been going on there for some time). Its director is Dr. R. F. Woolmer, and he has been appointed to the new professorship. The department is financed entirely by contributions from industry, and this latest gift is a striking reminder of how much the development of medicine owes to far-seeing and public-spirited people in the industrial world. The director is free to develop whatever research he thinks fit: by contrast to the practice in some countries, the industrialists financing the research do not impose any conditions on how the money is to be spent, which is administered by the Faculty of Anaesthetists. This is a timely as well as a generous gift, for anaesthesia is developing so fast that ideas worth pursuing are tending to outstrip the pursuers.

ROYAL SOCIETY FELLOWS

Two medical men are among the twenty-five scientists elected Fellows of the Royal Society last week. They are Professor Alexander Haddow and Professor A. St. G. McC. Huggett. As director of the Chester Beatty Research Institute at the Royal Cancer Hospital, London, since 1946, Professor Haddow has a key position in the large team of research workers there attacking the problems of cancer by every available device—physical, chemical, biological. His own research work has been largely devoted to the discovery of chemotherapeutic agents which will be toxic to the cancer cells but not to the host cells; among those compounds which have had some clinical success are the nitrogen mustards. In notably difficult terrain he has succeeded in effectively engaging the enemy, but the final outcome of this as of many other battles with cancer may not be seen for some years. Professor Huggett, who has been professor of physiology at St. Mary's Hospital, London, since 1935, has made a special study of the transfer of nutrient substances from mother to foetus through the placenta. He is well known for his many researches into the physiology of the foetus and the effect on the foetus of changes in the placenta.

Among the new Fellows are several non-medical scientists whose work has brought them into close touch with medicine. Dr. Edith Bülbring, a pharmacologist at Oxford University, has for some years been studying metabolism in muscle tissue and the electrical and chemical properties of smooth muscle. Dr. E. P. Abraham, of Oxford, has investigated various antibiotic substances, including penicillin compounds and recently the fungal product cephalosporin. Dr. J. R. Baker, also of Oxford, where he is reader in cytology, has developed ingenious chemical methods for studying minute structures within the animal cell. Many medical men interested in microscopy will know of his forthright expression of views in questioning the existence of the Golgi bodies as they were originally conceived. Dr. M. Abercrombie, of the anatomy department at University College, London, is distinguished for his studies on the behaviour of cells in tissue culture, embryonic tissues, and wounds. He has been editor of the *Journal of Embryology and Experimental Morphology* since it began in 1953. Dr. R. K. Callow is an organic chemist at the National Institute for Medical Research, and is well known for his researches, extending over many years, into the biological activity of the steroid hormones, latterly those related to cortisone.

SIR GORDON GORDON-TAYLOR, 80

Sir Gordon Gordon-Taylor reached his eightieth birthday last week, on March 18. The *British Journal of Surgery* has commemorated this notable event in a "special Cordon-Taylor Birthday Number." Seeing the familiar figure walking briskly down the street in a cold wind, without an overcoat but always with a carnation in his buttonhole, the passer-by would not believe the master surgeon was 80 years old. But that is his calendar age. His mind and his spirit are as fresh and blithe as ever, and no surgeon to-day can yet surpass him as an orator for the great occasion. Gordon-Taylor has been more than a great master-craftsman and inspiring teacher of eager apprentices. He is a much-loved figure in the British Commonwealth of Nations, and his long life has been devoted to the ideals of his profession, sustained by him in speech and writing and action. This *Journal* has cause to be grateful to him for help in many ways and with especial pleasure wishes him many happy returns.

[1] See p. 781.
[2] *Brit. med. J.*, 1957, **2**, 245.

THE BRITISH CLINICAL STAGING OF BREAST CANCER

BY

MICHAEL HARMER, M.B., F.R.C.S.

Surgeon, Royal Marsden Hospital, London

The need to classify cases of cancer of the breast has long been recognized. Probably the first staging, which took into account the patient's age, the extent of the disease, and the histology, as well as lactation or pregnancy, was that of Lee and Stubenbord (1928). This was adjudged to be too unwieldy, and the staging which gained most acceptance was that of Portmann (1937, 1943). In this country the Manchester modification of the Steinthal staging (Paterson, 1948) has been most popular, but several centres—for example, Edinburgh and the Royal Marsden Hospital (formerly the Royal Cancer Hospital)—introduced their own modifications. There are to-day, in general use in Britain, no fewer than five similar but differing classifications, differing in sufficient detail to make the accurate comparison of series largely impossible.

In 1953 Dr. P. F. Denoix, of Paris, suggested a new approach to the problem, and this forms the basis of the present communication. It is not necessary to go into details of the discussions which have taken place at various international meetings in the past five years. It is sufficient to say that these have now reached a stage at which it can be expected that international agreement will certainly be achieved.

Three years ago letters were published in the *British Medical Journal* and the *Lancet* (Harmer, 1955) pointing out that the International Union against Cancer would be meeting in London in July, 1958, and expressing the hope that before that date British surgeons and radiotherapists would meet, argue, and agree upon a clinical staging so that this country at least could speak with one voice in any international discussion.

A Joint Committee

The suggestion gained wide approval, though this was tinged with some scepticism. In the event, the Association of Surgeons and the Faculty of Radiologists agreed to sponsor the idea, and the council of each body delegated five representatives to serve on a committee to thrash out the matter. Mr. Richard Handley, London, was elected chairman, and the other members of the committee were: Mr. Hedley Atkins, London; Dr. George Blomfield, Sheffield; Professor John Bruce, Edinburgh; Mr. Michael Harmer, London (secretary); Dr. Ralston Paterson, Manchester; Mr. Victor Riddell, London; Professor David Smithers, London; Professor Robert McWhirter, Edinburgh; and Dr. Ivor Williams, London.

In his introduction to the memorandum which was finally submitted to the Association of Surgeons and the Faculty of Radiologists, Mr. Handley wrote:

"The staging of breast cancer is an attempt to formulate the extent of the disease. By staging, it is hoped to sort patients from different centres into comparable groups and thus to be able to compare the effects of treatment. It is also hoped that staging may help to guide treatment in individual cases and will give some indication of prognosis.

"Staging may be done on a clinical or a pathological basis. Surgeons, in recording their results, have usually used pathological criteria for staging because they believe them to be more accurate. At the present time there is a swing towards more conservative treatment, and there are thus many patients for whom adequate pathological data are not available. For these and other reasons, therefore, the staging of breast cancer on clinical grounds is of increasing importance. *It must be emphasized that this report deals only with clinical staging.*

"The Committee is well aware that clinical staging is inaccurate. It takes no cognizance, for example, of tumour malignancy or of host resistance. It is impossible to be accurate in the examination of the axilla, and the more obese an axilla the more inaccurate its clinical examination. Clinical examination can offer no light whatever on the state of the mediastinal lymph nodes. The Committee nevertheless believes that clinical staging, done in the manner to be detailed, is the best method available in the circumstances; that it is well worth doing, and that it is likely that some of the inaccuracies will be ironed out in large series of patients.

"Fundamentally there are four stages into which it would be desirable to divide cases of breast carcinoma: (1) where the tumour is confined to the breast; (2) where the tumour is confined to the breast and its axillary lymphatic drainage area; (3) where the tumour has spread beyond the axilla but is not generally disseminated; and (4) where there is wide dissemination."

Mr. Handley then went on to point out that several stagings already exist and that any recommendations for general adoption must be based on what has come to be called the TNM system, proposed by Denoix and approved by the Research Council of the International Union against Cancer (1956).

The TNM System of Staging

A few words explaining this system are necessary. It is based upon two principles, which may be applied to cancers at many sites but which are particularly suitable for accessible growths and therefore for carcinoma of the breast. These principles are: (1) The identification of cases comprising the group under study by assigning to each case certain symbols denoting the local extension of the primary tumour (T), the condition of the regional lymph nodes (N), or the presence of distant metastases (M). (2) The establishment of conventional stages, usually four in number, by grouping the cases according to the symbols allotted, which in turn indicate the progression of the lesion in regard to prognosis and the particular characteristics of each site.

It is the exact definitions of T, N, and M which are of cardinal importance in this system. This is only another way of stressing the importance of accurate note-keeping and recording of physical signs.

In fact, an accurate assessment of T, N, and M is of greater importance than the process of staging. Whereas the former is based on fact, the latter is an inference of what the facts mean. As experience accumulates, it may become desirable to alter the system of staging, which could be done retrospectively if T, N, and M had been defined in the necessary detail.

For cancers of the breast each component—T, N, and M—is subdivided into four gradations, according to its stage of advance. Thus T1, T2, T3, and T4 represent degrees of advance in the primary tumour, while Na, Nb, Nc, and Nd represent degrees of advance in the local lymph nodes. In subdividing the distant metastases into M1, M2, M3, and M4, it would be fairer to consider them as different categories, rather than degrees of advance, in a process which is already very advanced. Having defined the facts of an individual patient's disease in terms of T, N, and M, the clinician proceeds to the second step of grouping the resulting T, N, and M symbols into four stages, in such a way that the limited growths are in stages I and II and the advanced growths in stages III and IV.

At first sight all this may appear impossibly complicated, but a little thought should dispel such a gloomy impression. In fact, one is only asking clinicians to spend a little more time in recording the details of their patients' disease.

Proposals for Staging

The following proposals accord very well with those of the International Union against Cancer and are therefore, we believe, likely to be accepted. It would clearly be quite useless putting forward anything very different unless

British surgeons and radiotherapists were prepared to demand a system of their own.

The five basic principles which guided the committee in its recommendations were: (*a*) there should be four degrees of T, named T1, T2, T3, and T4; (*b*) there should be four degrees of N, named Na, Nb, Nc, and Nd; (*c*) there should be four degrees of M, named M1, M2, M3, and M4; (*d*) the definitions of these various TNM degrees should be clearly set out; and (*e*) the disease may then be staged in the conventional manner by grouping the symbols in a number of stages.

The Council of the Association of Surgeons and the Council of the Faculty of Radiologists make the following proposals for the definitions of T, N, and M and for the four stages.

Definitions

T: *T1* Skin fixation absent.
Pectoral muscle fixation absent.
Chest wall fixation absent (*Note 1*).

T2 Skin fixation incomplete (tethered or dimpled),
or Nipple may be retracted (in sub-areolar tumours),
or Paget's disease may be present.
Pectoral muscle fixation not complete.
Chest-wall fixation absent.

T3 Skin fixation complete (infiltrated or ulcerated),
or Peau d'orange present in tumour area,
or Pectoral muscle fixation complete.
Chest-wall fixation absent.

T4 Skin involvement or peau d'orange wide of tumour but not beyond the breast area,
or Chest-wall fixation present.

N: *Na* No homolateral axillary nodes palpable.

Nb (*i*) Homolateral axillary nodes palpable but not significant (*Note 2*).

Nb (*ii*) Significant homolateral axillary nodes palpable but movable.

Nc Homolateral axillary nodes fixed (to one another or other structures),
or Oedema of the arm.

Nd Homolateral supraclavicular or infraclavicular nodes movable or fixed.

M: *M1* Skin involvement wide of the breast, but no other distant metastases.

M2 Involvement of contralateral breast, axilla, or supraclavicular region, but no other distant metastases.

M3 Bone metastases only.

M4 All other distant metastases or any combination of M1, 2, or 3.

Notes

1. The chest wall includes the ribs, intercostal muscles, and serratus anterior muscle. It does not include the pectoralis muscles.
2. Lymph nodes are called significant if they are considered to contain growth.

Naturally, the question of the size of the primary tumour was discussed. It was felt that it would be difficult to include this in the definitions without adding further complexity, and it was argued that, if the size was included because of its influence on prognosis, then the situation of the tumour would also have to be taken into account. It should go without saying, however, that these two facts ought always to be included in the clinical description.

On the matter of the significance of axillary lymph nodes there has always been, and probably always will be, disagreement. It may appear clumsy to divide Nb into two categories, but it was felt that this could be done without prejudice to the definitions as a whole and therefore could be adopted or not by the clinician at will. It is a fact that lymph nodes may be palpable in the axillae of normal people, and palpable nodes in patients with breast cancer may be free of growth. The word "significant" is used to indicate that nodes are considered by the examining clinician to be malignant. As all staging is a matter of clinical judgment, this proviso was included only so that patients with insignificant nodes should be placed in an earlier rather than a later stage. After a great deal of attention had been given to this matter it was thought necessary to divide Nb in order to satisfy the views of those who believe that the significance of nodes can be judged clinically and of those who believe that all palpable homolateral nodes should be regarded as containing growth.

It was also agreed that when tumours are present in both breasts the definition should be M2.

It may be said that there is not much point in subdividing M. But already where this has been done on a small scale it has become apparent that there is indeed something to be gained from so doing. In some series it is surprising that the percentage of survivors in stage IV is so high, higher sometimes than those in stage III. The reason is that these survivors may be M1 cases where the disease, though extensive, is in fact still localized and may respond well to hormone therapy. Again, a solitary bone metastasis (M3) may be the only evidence of spread and may be treated with success. The division of M does therefore allow the comparatively few survivors in stage IV to be analysed.

Stages

Stage I: Skin fixation absent (T1) or incomplete (T2).
Nipple may be retracted (T2) or Paget's disease may be present (T2).
Pectoral muscle fixation absent (T1) or not complete (T2)
Chest-wall fixation absent.
No homolateral axillary nodes palpable (Na).

Stage II: Primary tumour as in stage I (T1 or T2).
Homolateral axillary nodes palpable but movable (Nb (i) or Nb (ii)).

Stage III: Skin fixation complete (T3) or skin involvement wide of tumour (T4).
Peau d'orange present in tumour area (T3) or wide of tumour (T4),
or Pectoral muscle fixation complete (T3),
or Chest-wall fixation present (T4).
Homolateral axillary nodes fixed (Nc),
or Oedema of arm (Nc),
or Homolateral supraclavicular nodes movable or fixed (Nd).

Stage IV: Skin involvement wide of breast (M1),
or Involvement of contralateral breast, axilla, or supraclavicular region (M2),
or Bone metastases (M3) or other metastases (M4).

It may be objected that each of the stages as set out above includes several different sorts of growth. For instance, stage I includes not only the very "early" cases but also some of those which by most standards are considerably more advanced—that is, where the growth is beginning to invade the pectoral fascia as shown by "incomplete fixation."

Again, stage III contains cases which may be locally advanced but otherwise not disseminated as well as those with fixed supraclavicular nodes which are usually included with stage IV.

The answer to such criticism lies in repeating that an accurate assessment of T, N, and M is of greater importance than staging. Unless a larger number of stages than the conventional four is to be adopted, then numbers of dissimilar patients are bound to be grouped together. If the stages are much subdivided, then in effect the particular stage becomes identified with a particular T, N, or M connotation. Thus a clinician interested in the survival rates of patients having really limited growths would describe the features not of stage I cases but of T1Na cases; and all his colleagues would instantly understand what he meant.

Four stages, however, do form a convenient means of grouping patients, and in any publication dealing with the TNM method it is usual to add a simple table indicating the various stage groupings. Thus:

Stage 1: T1Na T2Na
Stage 2: T1Nb T2Nb
Stage 3: T3Na
T1Nc or Nd T2Nc or Nd
T3Nb or Nc or Nd T4Na or Nb or Nc or Nd
Stage 4: Any combination of symbols including M.

Discussion

Such are the proposals relating to the staging of carcinoma of the breast. It must be emphasized again that these are based on a general system which commands international support and on particular definitions which already have the approval of the International Union against Cancer and which are to be discussed at the Seventh International Cancer Congress meeting in London in July.

British surgeons, perhaps more so than radiotherapists, are on the whole unaware of the TNM system of staging, and the committee is particularly anxious that as wide publicity as possible should be given to it before the Congress meets. To this end it is being published with the title of the *British Clinical Staging of Breast Cancer*. It is hoped that this article will stimulate discussion and criticism. It is further hoped that whoever is asked to speak for Britain in the committee appointed by the International Union against Cancer to discuss the matter will have the backing of surgeons and radiotherapists throughout the country.

Summary

A clinical staging of breast cancer is described.

This is based on the TNM system described by Denoix, of Paris.

There is no suggestion that these proposals should be adopted at this moment. But an attempt to gain international agreement on this matter will be made at the Seventh International Cancer Congress meeting in London in July.

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Correspondence

Because of heavy pressure on our space, correspondents are asked to keep their letters short.

Serial Cholecystography

SIR,—As nobody else has done so, I should like to comment on the article on serial cholecystography by Mr. J. Dudfield Rose (*Journal*, February 15, p. 360). The method described involves the use of 19 *x*-ray exposures. I have obtained measurements of the surface dosage which would be received by a patient of average size during this examination. The dosage amounts to 88½ roentgen units.

The International Committee on Radiation Protection has recommended that the total dose in *10 years* shall not be more than 50 r.u. Three out of four of the cases quoted in the article were women still within child-bearing age. The exact implications are rather complicated, but there is sufficient in the simple facts to cause us to consider seriously whether such a procedure is justifiable.—I am, etc.,

Stoke-on-Trent. C. BELLAMY.

Disease Education by the B.B.C.

SIR,—Tuberculosis in our hands! Is the B.B.C. determined to avoid all mention of sane prevention if there is no element of the cruel or the gruesome? No mention of adequate sleep, a good meal instead of tea and cigarettes, exercise in the fresh air, open windows at home and at work, guarding the mouth when coughing, forbidding spitting in public places? A glancing murmur only about active immunization, a cruel dissertation on the dangers of keeping one's elderly relatives at home—much safer away in an institution. And the rest—first catch your tuberculosis, have it diagnosed early, and "so long as you always take your pills, dear, you'll be all right." Balderdash—no wonder the doctors wish to remain anonymous.—I am, etc.,

Cromer. A. HENRY GREGSON.

SIR,—Although I have no television set of my own, I managed to see several of the programmes from *Your Life in Their Hands*. I am convinced that television is a very valuable medium which has come to stay, and therefore must be used to advantage.

The programmes I have seen, on the whole, have been presented well, but in my opinion emphasis has not been placed sufficiently on the preventive side of medicine. Very excellent diagrams of the airway and oesophagus were shown in the programme on poliomyelitis, and also the highly technical manner in which the airway was maintained by means of a cuffed endotracheal tube in bulbar cases. Since inhalation of regurgitated stomach contents is one of the commonest causes of death under anaesthesia, I feel it was an opportunity missed not to have stressed the importance of abstinence from food or drink for at least three hours before administration of an anaesthetic. What a change it would be if the patient were to volunteer that he had had food instead of one having to cross-question him at great length on this subject.

I was very interested in the programme from Edinburgh, but what a pity the head injury described was said to have been sustained on the football field! What a lot of good might have been done if more had been said about head injuries of a serious nature due to motor-cycle accidents! Everyone working in hospitals is familiar with the large number of surgical beds occupied by patients suffering as a result of this sort of accident.—I am, etc.,

Maidstone, Kent. SILVIA W. PYDDOKE.

SIR,—After reading the various conflicting opinions about the series *Your Life in Their Hands* one can only quote the old Latin tag *Quot homines, tot sententiae*. However, of what value is the opinion of some medical pundit who rarely comes into contact with the general public? His may possibly be *vox dei*, but is it necessarily *vox populi*? One has very little means of ascertaining. To ask casual patients gives little real indication. To the many people who attend hospital all the voices they hear there are *voces deorum*, even that of the newly qualified houseman, and they would only express an opinion which they thought would be in keeping with that of their mentors.

Many years ago when I first qualified I used to try to teach young mothers who could not feed their babies themselves the method of modified cow's milk as taught by the distinguished paediatrician of my teaching hospital. Only very few of the more intelligent carried out my instructions, the rest merely going away and buying a tin of condensed milk. There must be many doctors like myself who, as a sort of corollary to any advice they may give their patients as to their existing illness, often try to explain to them the nature of it, as well as how to prevent it if possible in the future. To the more intelligent this is obviously welcome, but in the case of others like the foolish young mothers referred to above one felt that they were merely saying to themselves, "Oh! cut the cackle and get on with the cure."

The public are quite disease-conscious enough as it is. After all, in spite of all the cancer propaganda we have had for years, women still come in with hopelessly inoperable cancer of the breast, and ignore advice about returning if a uterine haemorrhage does not clear up in a week or two, and these are often relatively young women in the 50's. Moynihan used to say, "We mustn't frighten people to death, we must frighten them to life." The reason usually given for delay in these women is almost always the same—the fear of operation. Will the present series do anything to banish this? I much doubt it. Many

people, especially women, live a not so very subconscious life of fear of cancer, which in my humble opinion will only be enhanced.

Whether it is a good thing or a bad thing, it is clear that medicine is becoming increasingly everybody's business, and the opinion as to whether it is a good or a bad thing is as valid whether it comes from a general practitioner or from the dean of a medical school. I, for one, am glad that I am much nearer the end than the beginning of my career as a doctor, for "when everybody's somebody, then nobody's anybody."—I am, etc.,

Brighton, 5. G. L. DAVIES.

Television Casualties

SIR,—So another patient has fainted whilst watching the programme *Your Life in Their Hands*, and the B.B.C. are accused of playing up to and pandering to the public. What was to prevent the patient turning her head away before fainting, or, better still, switching off the television set or not even looking at the programme at all? As for accusing the B.B.C. of sensationalism, why should not they televise what they see fit? After all, they have their business to run and have their own censors and advisers, who are no doubt experts in their jobs, just as we have specialists in our profession. How would the medical profession like to be told by outsiders how to treat their patients? It is one of the many duties and responsibilities of the B.B.C. to enlighten the masses in everything concerning them, and that surely includes matters relating to their health, especially when this is done with the closest co-operation of medical experts.

At one time the practice of medicine was to some extent associated with superstition and "hokery pokery," but the time has now come when members of the public—that is, our patients—refuse to remain in complete ignorance as to what is what in times of illness and demand to be enlightened—a very healthy attitude indeed, even though it may prove at times awkward for the doctor.

Now let us look at the other side of the picture. A female patient of mine who has been suffering from valvular disease of the heart for many years had repeatedly refused to undergo the advised appropriate operative treatment, but after seeing the operation on television came to me of her own accord, and, with a look of hope in her eyes and full of expectancy, insisted that I should go ahead and arrange for her to undergo the operation, which I have done. She voluntarily explained that her refusal in the past to submit to the operation was based on her own ignorance coupled with the gruesome stories told by her neighbours and friends, but after viewing the operation the fear of the unknown had completely vanished and at the same time her respect and admiration for the skill and grave responsibilities of the medical profession were greatly enhanced.

Let us be honest. The crux of the matter is this: human beings at all times sensationalize and magnify out of all proportion any adverse reaction in everything and anything, and that includes doctors and the field of medicine. Millions of people clamour to see and hear horror pictures and plays, etc., without any real harmful effects on their health. Local authorities hold exhibitions and show films illustrating and emphasizing the horrors of accidents in our streets and homes. Health authorities throughout the world focus public attention on the catastrophes of famine, cancer, tuberculosis, etc. The national press plays up and stresses the ghastliness of the H-bomb. Must all this highly educational propaganda be stopped because of the squeamishness of the few who unfortunately cannot take it? Certainly not.

Must we condemn this programme because it is new; because of the somewhat dubious untoward reaction it may have on a comparatively few individuals? I hope not. The human mind readily adapts itself to new ideas, from sack skirts to sputniks. Gruesome, we may say, as we look in at television, but within a short time it becomes part and parcel of the human curriculum. In the field of medicine to-day's precedent is to-morrow's routine, and in my opinion the B.B.C. have made history and given hope and courage to millions. If some international figure or a member of the Royal Family gave his or her public approval of this programme, then everyone, including the medical profession, would accept it as the "right thing." Did we not get the same condemnation and criticism by a minority of our profession regarding vaccination against smallpox and tuberculosis at the beginning; when chloroform was first introduced; operation for appendicitis (until it was made fashionable by royalty)?

Speaking for myself, and many of my colleagues and patients, we have nothing but the highest of praise and respect for all concerned in this controversial programme; and, for those who denounce it, may I remind them of another programme, *Time Marches On*?—I am, etc.,

Glasgow, S.W.3. ARNOLD B. COWAN.

SIR,—May I report another sort of television casualty? A little girl of 11 came to hospital with a greenstick fracture of her arm. She watched the nurse getting the plaster trolley ready, and then said: "I wanted to be a nurse." We asked her if she still wanted to be one, and she replied: "Not now. I saw that operation on the 'telly,' and I could not stand it when he put his finger right in the heart. I do not mind a growth, but I could not do anything like that."

She is probably an avid fan for the television medical series now running—and, though the sensible remedy for turning off such programmes when children are watching lies in their parents' hands, I wonder how many do.—I am, etc.,

London, S.W.10. G. COHEN.

"Diminished Responsibility" Manslaughter

SIR,—Dr. Patrick G. McGrath's letter (*Journal*, March 15, p. 641) on the question of "diminished responsibility" offers scope for criticism. To a person found "guilty but insane" it means many years, and often a lifetime, of imprisonment amongst "insane criminals" as an "insane criminal." His stigma is that of murderer. The privilege of receiving treatment or of having a "cure" effected must indeed be a doubtful one for such a person. If he ever emerged into full freedom it would be with the knowledge that he is still a murderer, though now a sane one.

A person found guilty under the "diminished responsibility" plea is stigmatized neither as murderer nor as insane. His punishment certainly may be lifelong imprisonment, but on the other hand his sentence comes up for revision every two years. Moreover, should the judge wish to show his personal concurrence with the jury's verdict he can do so by adding a rider of his own which may well influence revision in the prisoner's favour.—I am, etc.,

Kingswinford, Staffs. W. A. O'CONNOR.

Antibiotics in Influenza

SIR,—The February issue of *Prescribers' Notes*,[1] dealing with the question of antibiotics in influenza, stated that intramuscular penicillin was found to be effective against secondary bacterial invasion in certain groups of patients and favoured in many hospitals, but presented difficulty in general practice during epidemics, thus requiring oral therapy. I was surprised to note that no mention was made of penicillin V with or without sulphonamides.

There is now a great deal of evidence published that this is a dependable and economical form of therapy and that peak blood levels can be obtained in the fasting patient within an hour (e.g., Brown *et al.*[2]). On theoretical grounds it appears preferable to use penicillin V alone or combined with sulphonamides for all the indications mentioned in *Prescribers' Notes*, with the exception of the fulminating case, and to keep other antibiotics in reserve for cases which do not respond rapidly or adequately. My own experience in the two recent epidemics supports this view, and I am preparing a short memorandum of my results

obtained with penicillin V–sulphonamide oral therapy in general practice which I hope to submit for publication shortly.—I am, etc.,

London, S.W.6. WILLIAM P. GRIFFIN.

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Accidents from Gas Fires

SIR,—I have always thought that the practice of leading coal-gas into domestic premises, introduced near the end of last century, was an amazing and almost incredible event. It is still possible for the toddling infant to introduce tragedy into a home; also for the aged, the sick, or the rotund—sometimes an unhappy trinity in one individual who may almost have to invert himself to turn the tap of a gas-fire and then may fail to light the escaping gas before being overcome by a temporary attack of faintness, which could thus prove fatal.

To counter these possibilities could not the continued escape of gas be prevented as follows? No gas would be allowed to escape from a supply-pipe to a gas-fire, the tap of which had been turned on, except for a short prescribed period while the tap, under pressure of a spring, was returning to its closed position. If, during this period, the gas was ignited, the tap would be prevented from fully closing by the operation of a quick-acting bi-metallic thermostat. The gas-tap could then be turned to the required position. If the supply of gas to the fire were cut off by a failure of supply from the mains, or at a slot-meter, the tap would again move to the closed position and prevent any subsequent escape of gas on a return of the supply.

Further, I cannot quite understand why the heating element of a gas-fire should be so near the floor, where it is dangerously close to the flouncing portion of garments. The grilles are not an entire protection against fire.—I am, etc.,

Bradford, Yorks. ALLEN GLENN.

Pressor Agents or Steroids?

SIR,—Your leading article "Steroids and Pancreatitis" (*Journal*, February 8, p. 333) is stimulating, and, together with the paper by Drs. O. Garai and K. Shirley Smith on the use of pressor agents in shock in mycardial infarction (*Journal*, February 1, p. 247), provokes a mere surgeon into begging space to put forward some observations.

The same shock syndrome has been observed to occur in association with a variety of lesions. In essence this syndrome consists of a state of severe shock which persists in spite of the more usual therapeutic measures. The blood pressure is of the order of 60/30 mm. Hg and there is some cyanosis, particularly of the extremities. This clinical picture has been observed following abdominal operations, particularly gastrectomies; in conditions of trauma (not overtly serious) in the region of the upper lumbar vertebrae; in acute pancreatitis; in myocardial infarction and mesenteric thrombosis. In some instances, according to Illingworth and Kay,[1] this syndrome, following gastrectomy, has been associated with a final diagnosis of necrotizing enterocolitis. Except *post mortem*, such a diagnosis must be difficult to make; and on the whole it seems more likely that the vascular collapse may give rise to necrotizing enterocolitis than that the latter condition creates the shock syndrome under discussion.

In all instances of the syndrome quoted, it seems significant that the areas involved are associated with an abundant autonomic nerve supply. It is not unreasonable to postulate that the syndrome might result from a nocuous stimulus to the autonomic system leading to dysfunction or perverted function of the adrenals or the cerebral centres of autonomic function. Some support is given to this view in the light of successful treatment of the syndrome with L-noradrenaline.

The syndrome as seen post-operatively may mimic very closely the clinical condition of myocardial infarction. As the electrocardiogram may not show any diagnostic change for some hours, it is a relief to learn, on the authority of Drs. Garai and Shirley Smith, that treatment with pressor amines is indicated even for myocardial infarction. Undue delay in treatment of the syndrome will lead almost certainly to imbalance of the internal environment and to irreversible shock.

In my experience treatment by pressor amines alone is enough. The indication and necessity for the administration of steroids have yet to be proved; and steroids are not without danger, if only from the point of view of wound dehiscence. Electrolytic imbalance seems to be a later manifestation of the syndrome and not a cause. The role of antibiotics, particularly as applied to the treatment of acute pancreatitis, is difficult to assess. Apart from the fact that there is no proof of infection, as the term should be understood ordinarily, there seems to be increasing alarm and confusion over the use of antibiotics at all in acute abdominal surgery. A final observation on treatment with L-noradrenaline is that, after some hours, a sort of tolerance may develop necessitating an increased dose to maintain the blood pressure. I can, however, confirm the value of ephedrine in restoring the potency of the L-noradrenaline, as described by Muggoch and Dwyer.[2]—I am, etc.,

London, W.1. J. S. CALLCUTT.

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Breast-feeding

SIR,—I am surprised that there have not been more letters in favour of breast-feeding in view of the article by Drs. F. E. Hytten, Jessie C. Yorston, and A. M. Thomson (*Journal*, February 8, p. 310). Surely there is nothing better than successful breast-feeding for the mother and child. Complementary feeding is not satisfactory, having the disadvantages of both methods, and should not be persisted in if there is little chance of the baby becoming entirely breast-fed. In my limited experience many mothers give up breast-feeding when they get home, not because it has been unsatisfactory but because they are against breast-feeding and had intended to bring up their baby on the bottle all the time. They are often very reluctant to admit this. I quite agree that, if these mothers cannot be persuaded of the advantages of breast-feeding, it is better that the baby should be started on the bottle to begin with. This matter should be discussed and decided on during the antenatal consultations.

Surely it is not necessary to list all the many mistakes that a large number of mothers make with bottle-feeding. These mothers are frequently frustrated, anxious, and unhappy, and the baby far from contented until the general practitioner has been able to sort out the problem and put matters right.—I am, etc.,

Gillingham, Kent. C. A. RUSHMER.

SIR,—Dr. Grantly Dick-Read hastens to reassure the wider circle of readers that "the majority of men and women in the British Isles will resent the implications in this [Aberdeen] report." The implications are (see *Journal*, February 8, p. 310) that from out of a cross-section of mothers conditioned by a mid-20th century urban environment the great majority encountered difficulties in breast-feeding that converted an ideally highly satisfying, natural function into anxiety relieved only when bottle-feeding was resorted to.

The subject of breast-feeding is highly charged with emotions while our scientific data in themselves carry little evidence that might substantiate extremist attitudes. Unconsciously, however, we are one and all possessed by the concept of "participation mystique," one of whose images is the babe at the mother's breast, symbolizing the ideal ecstasy the mature woman experiences in her surrender to motherhood. On this level the bottle is experienced as the "rejecting mother," and therefore as "bad"; and "bad" we must continue to experience it until we learn

to acknowledge the power these images have in determining our so-called attitudes.

Having now (at least on paper) relegated emotional contexts of the controversy to their rightful origins, can we not bring ourselves to examine a little more dispassionately to what extent "natural motherhood" is possible or expedient in a highly artificial society? In the "natural" society, no duties are imposed on the lactating mother (the Aberdeen report substantiates the benefit two women similarly placed derived). The baby can be put to the breast in public or, if not, privacy is assured. The "natural" mother has never been a clockbound precision worker. And, perhaps most important, she has never before been as isolated in her own four walls, with all the terrors that a crying baby can arouse, as to-day. In this state, it is no consolation that one can go to the clinic to-morrow or sit in the doctor's waiting-room to-night, "feeling an awful fool," when what is needed, and what the State cannot replace adequately, is the older, experienced woman who in a "natural society" is always present to reassure or take over at the inevitable critical moment.

Must we not then, being what we are, re-examine the premises of "the bad, rejecting mother who can only offer substitutes and second bests"? The alternative may well prove to give potentially excellent modern mothers a feeling of inferiority and guilt that must alienate them from the child, whereas it can in no way alter the social realities conducive to "the bottle." By all means let us attempt to arrange optimum lactating conditions for those who want to be helped to them, or those who would like "to try," but let us no less enthusiastically support the right of the differently conditioned mother to enjoy *her* motherhood with the reassurance she will derive from weights and measures. There may well be a swing of the pendulum towards a way of life less traumatic to all our human needs, and none would welcome it more than I, but in the meantime we shall only help one another and ourselves by humbly seeking to understand, instead of condemning manifestations of the moment. Perhaps we are less bad than we think.—I am, etc.,

London, W.11. ELEANOR ETTLINGER.

SIR,—It was left to Dr. R. N. Compton Smith (*Journal*, March 8, p. 581) to mention the real difficulty about infant-feeding. A girl is shy of putting a baby to the breast, even before her mother-in-law: yet if the same girl spent the day half-naked on a crowded beach, no one would bat an eyelid. A few film-stars appearing on cinema and television screens suckling their babies might do more to correct this anomaly than all the efforts of the Health Services.—I am, etc.,

Isle of Wight. N. P. BRUCE.

Artificial Insemination

SIR,—I read with interest Dr. Sheila Wood's letter on A.I.D. (*Journal*, March 8, p. 582), as it represents a familiar opinion. Her solicitude for the emotional welfare of a childless wife of an unfertile husband provides, however, a convenient channel for the emotional cowardice which epitomizes this "enlightened" age. If a woman feels an urge for a child so great that consideration for her husband will not quell it, then let her admit to her need and have a child by the more usual means and go out to work to keep it. One cannot have everything.—I am, etc.,

London, S.E.15. H. J. ANDERSEN.

SIR,—There are three points on which I must join issue with Dr. Sheila Wood (*Journal*, March 8, p. 582). First, I feel that most right-minded men and women including the vast majority of infertile couples, can and do judge the "merits" of A.I.D. far better than those who become emotionally involved, either personally or professionally. A.I.D. may give an individual, or couple, a desired result, but only at the cost of secrecy, deception, conspiracy, fraud, and a breach of the marriage contract.

Secondly, a woman to whom the denial of pregnancy would mean "the total failure of [her] existence" is both emotionally and spiritually immature; not just endowed with a highly developed maternal instinct, as Dr. Wood suggests. A woman whose life is centred solely round her reproductive function puts her whole reason for existence on the purely animal level and is in sore need of both psychological and spiritual guidance.

Lastly, I am convinced that an adopted child is as precious to a normal mature woman as one she has borne herself: even where a natural child of the marriage has followed on an adoption. Where adoption has failed the cause has been either the method by which it was arranged (e.g., direct adoption) or faults in the adopters themselves, both of which are happily preventable in adoptions arranged through a society of proved merit. The adopted child, unlike that born of A.I.D., bears an equal relationship to both parties of the marriage. Their love and relationship are further enriched by the fact that an open and honest explanation to the child, from its earliest years, is a *sine qua non* of a successful adoption. Only foolishness and weakness in concealing the facts lead to disaster in the relationship—a danger which is obviously all the greater in a case of A.I.D., since the truth cannot be told without disastrous results, while concealment results in a permanently false and dishonest relationship to the family and to the community. I speak as an adopter, as an Anglican, and as a practitioner with long experience of investigating and, I hope, helping childless couples.—I am, etc.,

Upton-by-Chester. HORACE INGHAM.

Tetanus

SIR,—We have read the papers by Dr. D. D. Johnstone and Drs. R. S. Packard, T. B. Cartmill, and J. G. Henry on the treatment of tetanus (*Journal*, January 4, pp. 12 and 16) with great interest. No one could reasonably dispute the importance of assessing prognosis before deciding the method of treatment.

According to Cole[1] the period of onset is the best prognostic yardstick, and Dr. Johnstone states this is usually more accurately measured than the incubation period. But is it? Our difficulty in this hospital (the General Hospital, Penang) has been to define what is meant by the term "generalized spasm or convulsion" so that the crucial onset period may be estimated (and so that the attending nurses and doctors know what they—and others—are writing about when they record such events). Cole described a reflex spasm as consisting of the following: (1) The whole body suddenly becomes rigid; (2) the jaws are tightly clenched; (3) the neck and trunk are arched backwards; (4) the limbs are extended; (5) the patient foams at the mouth and becomes cyanosed; (6) respiration may be stopped. The severity of these spasms can be graded according to duration (few seconds to three or four minutes), frequency, and whether they occur spontaneously or only follow a precipitating factor. This is an admirably concise description which might well be adopted as the criteria of a "generalized spasm" (although the severity remains to be defined). But in patients observed here there has appeared to be an infinite variation—in extent—from a local twitch involving, say, the hand only or the neck to the full-blown spasm with the six components enumerated. At what stage do these "minor" spasms qualify for the term "generalized"? Patients have been observed to die during or immediately after a spasm in which no limb extension, frothing, or cyanosis was seen. Are such spasms "generalized"? In many instances the patient is admitted after the onset of spasms, and in these cases it is virtually impossible from the descriptions available to estimate the period of onset with any accuracy if the five criteria have to be fulfilled.

Doubtless the period of onset if clearly defined is helpful in retrospective grading of cases, but is it reliable in assessing individual patients on or shortly after admission? Dr. Johnstone says it is not justifiable to use hazardous methods of treatment in "mild" cases. Yet one-third of his "mild" cases ended in death. To us it is often difficult to explain why some patients survive yet others die. Excluding fulminating toxaemia, the two main lethal factors seem to be chest infection and spasms. In pre-

venting chest infections, we believe the prone position is all-important. "Keep them off their backs" should be the constant watchword to nurses, who may not remember that the trachea runs backwards and that unconscious or drugged patients on their backs will therefore retain respiratory secretions which can become infected in a few hours. Inhalation of vomit is much less likely to occur if the patient is lying prone. We are convinced this simple manœuvre is much more important to the patient than "preventive" antibiotics, "frequent turning," "laryngeal toilet," etc. Another excellent reason for "keeping them off their backs" is lessening the danger of phlebothrombosis, particularly in the soleus intramuscular veins. Gibbs[2] showed this to be the most common site of phlebothrombosis and noted that dependent drainage here will be obtained when the patient is lying prone.

Prevention of spasms can only be achieved with certainty by relaxants such as curare. But this automatically entails artificial respiration with all the complexities, strain on medical and nursing staff, etc. If one advocates such a regime for severe tetanus, what are to be the indications for adopting it in a particular case? Is it to be the first "generalized spasm" as defined above? A patient recently observed died in the first such spasm. Is failure of conservative methods to be the criterion? Another patient was admitted with frequent spasms which were apparently controlled satisfactorily by thiopentone and chlorpromazine. On the fourth day, without any obvious warning, he then had a general spasm and died. If curarization and intermittent positive-pressure artificial respiration (I.P.P.R.) regime is started, when should it be stopped? One patient with a 24-hour onset period was treated by the respiration unit here for 13 days with the I.P.P.R. regime, but continued to have general spasms for 48 hours after the machine was stopped. Are such spasms hazardous to life even though the intoxication is on the wane?

There are so many questions to which there seems no satisfactory answer. Indeed, there are so many variables in tetanus that the greatest caution is needed in concluding any particular line of treatment is an advance—for the patient. Creech and his colleagues,[3] in a masterly review of probably the largest published series ever treated in one hospital, showed a falling trend in mortality interrupted by "bad years" over the last 50 years, a fall rather similar to tuberculosis before the days of streptomycin and isoniazid. The trend could not be convincingly correlated with any of the so-called advances such as antiserum, sulphonamides, antibiotics, tracheotomy, or gastrostomy. In 1949 they had 19 successive patients, all of whom recovered. As they remark, if some new treatment had been tried out during these admissions, it would have been tempting to attribute the success to the innovation. But the final mortality for that year was higher than any other year from 1946 to 1956. Dr. Johnstone had the courage to withhold antiserum. Would it be justifiable to withhold sedative drugs as well? How many patients are killed by the "treatment"?—We are, etc.,

H. A. REID.
D. P. BOWLER.
L. T. SCOTT.

Penang, Malaya.

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1 Cole, L., *Brit. med. J.*, 1953, **1**, 150.
2 Gibbs, N. M., *Brit. J. Surg.*, 1957, **45**, 209.
3 Creech, O., Glover, A., and Ochsner, A., *Ann. Surg.*, 1957, **146**, 369.

Aural Deformity and Renal Agenesis

SIR,—I wish to refer to the report by Dr. D. Hilson entitled "Malformation of Ears as Sign of Malformation of Genito-urinary Tract" (*Journal*, October 5, 1957, p. 785). Dr. Hilson's findings are of unusual interest, and are borne out in a report entitled "Bilateral Agenesis of the Kidneys," by Dr. James H. Duxbury.[1] A photograph in Dr. Duxbury's report (Fig. 1) of a profile view of the head and face of the patient under discussion reveals abnormalities of the ear strikingly similar to those noted in the patient pictured in Fig. 11 of Dr. Hilson's article. It is possible that Dr. Hilson has described an association of findings which, if confirmed by other reports of similar findings, might warrant permanent recognition and incorporation into the teachings of physical diagnosis.—I am, etc.,

GEORGE X. TRIMBLE.

California, U.S.A.

REFERENCE

1 Duxbury, James, *Canad. med. Ass. J.*, 1958, **78**, 123.

Acute Otitis Media

SIR,—There are some comments I would like to make relating to your leading article on acute otitis media (*Journal*, February 8, p. 328). You state that "few will disagree with F. W. Davison, who found that otitis media occurs more often in children with enlarged adenoids; experience in Great Britain would generally confirm that adenoidectomy prevents recurrences in a high proportion of cases." Earlier, however, you report that "such data as were obtained [by the M.R.C. Survey] on the significance of tonsillectomy and adenoidectomy in relation to recurrence of acute otitis media showed no difference that could be attributed to the operation." It therefore appears that the report does not justify your statement.

Secondly, you state that "the lower incidence of acute otitis media in adults is in part due to the atrophy of this lymphoid tissue [involving the Eustachian tubes], which usually takes place after puberty." This must surely be regarded as a very minor factor, since the dramatic decline in the incidence of acute otitis media occurs at about 7 years of age.—I am, etc.,

J. MCA. WILLIAMS.

Buxton, Derbyshire.

Research Workers and Pre-registration Year

SIR,—Professor L. J. Witts suggests (*Journal*, January 25, p. 222) waiving the pre-registration year for full-time research workers, who have, by implication, qualified in medicine to get more money. As an ex-student of his, without disloyalty, may I suggest that that is infamous? On qualification, it is now up to a prospective doctor to learn his job, and to prove that he can discharge it, in the compulsory pre-registration year. If in the future any of these half-fledged doctors have to practise medicine—for instance, in the unhappy event of an atomic war—I shudder to think of the consequences.—I am, etc.,

M. C. FFRENCH-CONSTANT.

Newquay, Cornwall.

Carpal Tunnel Syndrome

SIR,—Encouraged by the good results of treating stenosing tendovaginitis of the radial styloid and the trigger fingers with the local injections of hydrocortisone, I have during the last 18 months been treating cases of carpal tunnel compression syndrome by the same method. It was Nissen[1] who reported thickening of the flexor tendon sheaths in the carpal tunnel in cases of the syndrome and who suggested that this thickening might reduce the capacity of the tunnel and so compress the nerve. Phalen and Kendrick[2] observed thickening of the "flexor synovialis" in 70% of cases on which they operated. They too have treated 20 of their more recent cases with hydrocortisone injections, with good results in 16. In two of my cases treated by operation, granulation tissue was observed to be investing the tendons, and in others a thickening, as described by Nissen, was noted. It would appear therefore that a chronic tenosynovitis is the most likely cause of the syndrome.

Twenty-four cases of the syndrome have been treated by local injections of 0.5-0.75 ml. of hydrocortisone acetate into the tunnel. The needle has been inserted from the wrist at a point on the ulnar side of the palmaris longus tendon. Three patients were eventually operated on; the first, having osteoarthritis of the wrist and carpus, did not obtain any relief from the hydrocortisone; the other two obtained a dramatic response to the injections, but one was submitted to operation to find out why she could not flex her fingers fully, and this patient was one of those who had granulation tissue covering the tendons in the tunnel and in the finger sheaths. The symptoms of the third case recurred when she returned to work as a weaver on three or four occasions, and, having developed a phobia about injections, she asked for operative treatment.

Eight patients have been completely relieved for nine to eighteen months; four had only one injection, the other four had received two or three injections. Three cases have been relieved for periods between three and nine months; one relapsed slightly five months after his first visit, another ten months afterwards, but both responded to another injection. Seven patients have been completely free of symptoms for periods varying from one

to three months. Another four patients relapsed three months after the last of two or three injections. All responded to another injection, except one who refused a second injection. As mentioned above, another case chose operation.

When I began using hydrocortisone I gave one injection, repeating it only when the symptoms recurred. Latterly, however, I have given a short course of three injections at fortnightly intervals. Phalen and Kendrick[2] give weekly injections for three or four weeks. The dramatic relief which the patients obtain from the nocturnal pain (often described as "terrible," "searing," or "bursting") is most gratifying. Their description of the relief obtained varies, but "marvellous," "unimagined," and "wonderful" are words they use. It seems, therefore, that hydrocortisone may displace operation as the treatment of choice in this syndrome. —I am, etc.,

Burnley. DAVID A. RICHMOND.

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[1] Nissen, K. I., *J. Bone Jt Surg.*, 1952, **34B**, 514.
[2] Phalen, G. S., and Kendrick, J. I., *J. Amer. med. Ass.*, 1957, **164**, 5, 524.

Tuberculous Rheumatism

SIR,—I have read with interest the medical memorandum by Dr. Paul Mestitz on a case of tuberculous rheumatism (*Journal*, February 15, p. 383). Many years ago, as the result of a survey by the medical officer in charge of a large tuberculous population, four cases were sent to me with symptoms corresponding with those described by Poncet[1] as *rhumatisme tuberculeux ankylosant*. All of the cases were men in the middle period of life and were typical examples of chronic pulmonary tuberculosis; in three of them, tubercle bacilli had been found in the sputum. In each case, in addition to the pulmonary symptoms, chronic pain and severe limitation of movement were present in more than one joint, although the joints themselves showed no evidence of tuberculous disease.

I showed the cases at a local medical meeting, and I also read an account of them to a gathering of larger scope. More than one opinion was expressed. In accordance with one view, the association of tuberculous and rheumatic symptoms was thought to be a fortuitous one. In an alternative view, the cases were regarded as instances of Poncet's syndrome, and it was suggested that a severe tuberculous infection in a highly resistant subject might give rise to prolonged and widespread fibrositic reactions. A similar explanation might also account for the occurrence of scleroderma in a rare association with pulmonary tuberculosis.—I am, etc.,

Sheffield, 10. R. G. ABERCROMBIE.

REFERENCE

[1] Poncet, A. (1897). *Gaz. Hôp. (Paris)*, **70**, 1219.

Peroxidase and Catalase

SIR,—The article by Dr. K. A. J. Järvinen on "Determination of Peroxidase in Urine" (*Journal*, February 15, p. 379) appears to involve confusion between peroxidase and catalase. Measurements of both enzymes are very useful in medical and other branches of biochemistry, but they are different enzymes and are measured in different ways.

Peroxidase is an enzyme which decomposes hydrogen peroxide to give active oxygen which is capable of oxidizing suitable substances. In the common form of the test a few drops of 0.1% hydrogen peroxide and a few drops of freshly prepared 2% paraphenylenediamine hydrochloride are added to the solution, and if peroxidase is present a vivid blue colour appears in a few seconds. Perhaps the best-known application of this test is the classical Storch test for efficient pasteurization of milk. However, this can only be used to control the efficiency of high-temperature pasteurization as used on the Continent; it is useless for milk in this country, which is pasteurized by a low-temperature system.

Catalase is an enzyme which decomposes hydrogen peroxide to give ordinary gaseous oxygen, and is present in most tissues and cells. The volume of oxygen produced can be used as a rough measure of the amount of tissue or number of cells present. A well-known example is the detection of mastitis milk, which may contain well over a million cells per ml., whereas normal milk usually contains not more than 50,000.

Although special apparatus is available for measuring catalase activity a reasonably accurate estimation can be made by the following simple method[1]:

One ml. of 20 vol. hydrogen peroxide is added to an ordinary test-tube and the tube then filled to the brim with milk from the liquid under test. The tube is closed with a bung, through which is bored a small hole, in such a way that no air remains. The closed tube is then inverted in a beaker and left at room temperature overnight. The following morning the volume of gas in the tube is measured with a ruler. The test has no absolute significance, and therefore a control using a known normal milk or fluid should also be set up at the same time. The test is quite arbitrary, and the volume of oxygen can be measured after, say, three or five hours if this is more convenient.

This test has been found very useful as a preliminary means of detecting mastitis milk in dairy cattle and could doubtless be used to detect human mastitis. The size of tube can be adjusted as required.—I am, etc.,

London, W.1. J. G. DAVIS.

REFERENCE

[1] Davis, J. G., and McClemont, J., *J. Dairy Res.*, 1939, **10**, 74.

Knock-knee in Children

SIR,—Mr. Denis Browne in commenting on knock-knee in children (*Journal*, December 21, 1957, p. 1492) seems to illustrate again the fact that it is extremely difficult to eradicate old-fashioned ideas from medical thinking once they become established. Considerable evidence has accumulated in recent years, including Dr. A. J. M. Morley's work (*Journal*, October 26, 1957, p. 976), showing that when knock-knee occurs in a child who is otherwise normal it is extremely likely that return to straight alignment of the lower extremities will occur even without treatment. There are many statements in the older literature like Mr. Browne's to the effect that such cases require treatment. There are, however, no published cases, with careful clinical and radiological documentation to show any untreated cases in otherwise normal, healthy children, which have given unsatisfactory results. Until this is done, statements like his that there are "many unnecessary tragedies" do not add to our knowledge.

In connexion with a publication of our own on the same subject (in press), we have been unable to find in our own material or any of the published literature any case of knock-knee with malleolar separation of 4½ in. (11.24 cm.) or less occurring in an otherwise normal child which did not revert to normal, and this without treatment.—I am, etc.,

Montreal. J. S. DUNBAR.

Problems of Puberty

SIR,—I see that the subject of masturbation has once more risen to the surface in your correspondence columns. Dr. R. N. B. Byatt (*Journal*, February 15, p. 397) calls it a "revolting practice," which suggests he is not able to look upon it as dispassionately as is advisable. Through my work as a psychologist I have become firmly convinced that it is the vicious circle of act causing despair and despair causing act which leads to abnormal indulgence. A complete change of outlook and habit comes when the victim is given positive reassurance that he is not uniquely depraved and that he has not made himself unfit for marriage and paternity. With regard to the latter, I see many patients who find themselves impotent on the marriage night simply through anxiety which has resulted from this belief. —I am, etc.,

Scarborough. R. MACDONALD LADELL.

SIR,—I was disgusted with the pompous letter by Dr. R. N. B. Byatt (*Journal*, February 15, p. 397). It is not difficult to understand why so many adolescents who practise masturbation become neurotic and exhibit feelings of guilt if they are subjected to teachings such as Dr. Byatt would administer that masturbation is both a "revolting"

and "evil" practice. While I agree that Kinsey's figures of the percentage of the American population that masturbate is high compared with this country, he has shown that early orgasmic experience whether received by autosexual or heterosexual activity is beneficial to early sexual adjustment in marriage.

The analogy of self-control in the field of study which Dr. Byatt mentions is completely misplaced; self-control in this sphere is a means to an end which has its rewards. What he seems to fail to understand is that masturbation is the first rung of the ladder of sexual experience and only becomes harmful if it is practised to excess. I am sure that many medical practitioners would agree that abstinence accompanied by feelings of conflict and nervous tension is much more nocuous. Let us then not attempt to discourage masturbation, but rather to stamp out the foul distortions of its danger which are themselves most harmful. —I am, etc.,

Newcastle upon Tyne. M. T. SHAW.

Treatment of Helminth Infections

SIR,—I have read with great interest the articles, published in yosr issue of January 18, by Drs. L. G. Goodwin and O. D. Standen on the treatment of roundworms, hookworms, and tapeworms with piperazine salts (pp. 131–135). I would like to make the following comments.

For some time now, I have been treating ascariasis and ankylostomiasis in a highly infested area near Alexandria. I have found that, if ascariasis is treated with piperazine salts, whether adipates or citrates, in the form of one dose of 4 g., the treatment is likely to fail. Better results are achieved, however, by using something like 16 g. of piperazine spread over a period of seven days. The latter method is rather expensive and the failures under it may add up to about 40% of the cases treated. Practical considerations normally increase the incidence of failure still further, as the patient tends to miss one or two doses during the period of treatment.

As for ankylostomiasis, piperazine salts in my experience are quite useless for its treatment. For both ascariasis and ankylostomiasis, I have been using a combination of tetrachloroethylene and oil of chenopodium in the ratio of 6:1 with fairly good results. The amount should differ according to the age of the patient, the adult dose being 3 ml. and 0.5 ml., respectively. But there is obviously scope for a better drug.—I am, etc.,

Alexandria, Egypt. GAMAL EL SERAFY.

Antoine Bayle

SIR,—May I, through the courtesy of your columns, pay a tribute to the memory of a great French psychiatrist, the centenary of whose death is commemorated this week? He died on March 29, 1858. Perhaps because dementia paralytica has become a rare disease, the name of Antoine Laurent Jessé Bayle is less well known to the present generation of physicians than it was to their fathers. Bayle was the first to give a clear description and definition of dementia paralytica—or, as it is often called in his native country, *la maladie de Bayle*.

Bayle's fame rests chiefly on two works. The first, and the one that establishes his priority, was published in 1822 when he was only 23 years old; this is his doctrinal thesis entitled *Recherches sur l'Arachnitis Chronique, etc.*, and has been translated into English by Moore and Solomon.[1] The second, a substantial book of 600 pages, was published four years later and is the medical classic, *Traité des Maladies du Cerveau et de ses Membranes*. Its style is so limpidly clear that this book can be read with pleasure even by those whose knowledge of the French language is, like my own, very imperfect.

Bayle has been curiously neglected both by medical historians and by psychiatrists. His name is not mentioned in the histories of Garrison, Castiglioni, or Major, nor is it mentioned in a recent British textbook of psychiatry well-known for its emphasis on the physical factors in mental disease. Yet Bayle was one of the very first to assert, and to support his assertion with adequate evidence, that insanity may be due to pathological changes in the brain. In his insistence on the importance of pathological anatomy he followed the views of his uncle, Gaspard Laurent Bayle, and of his one-time chief, Laennec. Baillarger considered Bayle's work to be the most important single achievement in the history of mental disease; and as recently as 1922 the Neurological and Psychological Section of the British Medical Association, in sending their congratulations to the Dean of the Faculty of Medicine of Paris on the centenary of the presentation of Bayle's thesis, observed that "the discovery and differentiation of this disease (dementia paralytica) are justly regarded as one of the greatest advances ever made in the history of neurological and psychological medicine."

Bayle was not alone among his contemporaries in delineating dementia paralytica, and indeed the question of priority was for many years the subject of acrimonious debate. But from the vantage-point of more than a century we can stand above this dispute, and in honouring the memory of Bayle we may honour too that of his many brilliant young contemporaries—Calmeil, Georget, Delaye, and others—who drew their inspiration from the genius of Pinel and Esquirol. —I am, etc.,

London, S.E.5 E. H. HARE.

REFERENCE

[1] Moore, M., and Solomon, H. C., *Arch. Neurol. Psychiat. (Chicago)*, 1934, **32**, 804.

Anxious Patient and Worried Doctor

SIR,—I was interested to read Miss Madge Dongray's remarks (*Journal*, January 25, p. 220) and her thesis of a closer working relationship between doctors and social workers as an answer to the problem of the "anxious doctor." At present there are not many psychiatrically trained social workers, and only a fraction of these are working in the community health services. Even if these 50, say, men and women would whole-heartedly co-operate with doctors and the doctors with them it is too small a figure to answer the problem of the practitioner who needs such co-operation. But not all doctors would ask the help of social workers to take the burden off their back. In fact, I believe there are only very few medical practitioners who trust social workers. A partnership needs mutual respect and acceptance of equal roles. The status of the social worker is not equal to that of the practitioner. There are many doctors who would never hear of sharing their practice with non-medically qualified personnel. The experiment that Dr. Neville Davis and I conducted was rather an exception. I cannot say that I entirely blame the doctors for their suspicion. There are indeed many "odd birds" in the field of social work who could not offer anything but possible confusion. But increasingly highly qualified and conscientious social workers are entering the field, and a great many of the teachers of our profession have far-reaching vision and experience. At present we can only talk about isolated experiments like that of Miss Dongray's in Manchester, but great developments are needed before a noticeable change will manifest itself.

Perhaps I will be forgiven, Sir, for saying that the training of medical students did not and does not encourage such co-operation. From what I am told by my medical friends there is somewhat little training for psychiatry, psychodynamics, or in inter-personal relationships. Medicine in this country has had for centuries the greatest respect of the public. Up to the beginning of this century the patient looked upon the doctor as an angel of God, if not God himself. And, as doctors are only too mortal, some of them liked this omnipotent role. Why the poor unintelligent patient should want to know what was wrong with him was beyond the doctor's comprehension. When some years ago I went to the hospital for the result of an *x*-ray picture of my sinuses and asked the registrar for this result, he turned to me in surprise and asked, "Why do you want to know?" And in my bewilderment I could only answer the truth, "Because it happens to be *my* nose, sir."

In the last fifty years we have gone through a very great social change, and, while the public still reserves a special

respect for the medical practitioner, he is not now considered omnipotent any more. But to give up the omnipotent role is far from being easy. In my day-by-day work I meet patients who complain that they do not get satisfaction to their inquiries as to the nature of their illnesses from the doctors. The result is often a change of practitioner or else resignation on the patient's part and "passive resistance." This contributes to another kind of "anxious" patient, who suffers from a new disease, "doctoritis."

The change in the attitude of some doctors, the recognition of the importance of co-operation with other professions, will have to start in the medical schools where perhaps experienced and highly qualified psychiatric social workers could participate in the education of medical students, particularly in inter-personal relationships. Then it may become natural for the doctor of the next generation to share his knowledge with the patient for the patient's benefit, and to share the burden of his practice with social workers.—I am, etc.,

Edgware, Middlesex. EUGENE HEIMLER, Psychiatric Social Worker.

Rheumatology as a Whole-time Specialty

SIR,—I am of the opinion that the rheumatologist should be a physician concentrating on all branches of rheumatology, which will include an interest in orthopaedics, surgery of joints, endocrinology, psychology, pathology, physiochemistry, and manipulative treatment, continually following the advances in these specialties, but also keeping hold of the main basis of rheumatology, which is general medicine. This is a whole-time specialty.

The rheumatologist should be the "middle-man" between the general practitioner and the orthopaedic surgeon and the physiotherapist; but let him or her be a physician above all with a special degree or diploma in medicine. I am well aware that at international congresses and at meetings of societies such as the Heberden Society hundreds of "rheumatologists" forgather for discussion of the rheumatic diseases, but they are a mixed company of general physicians, orthopaedic surgeons, physical medicine, or pathology, or physiochemical specialists. There is not the "rheumatologist" as I should like to see recognized—a physician with his sole interest in the rheumatic diseases. I understand that the State does not recognize the specialty of rheumatologist. It is high time that such a specialty should be recognized by everyone.—I am, etc.,

London, W.1. M. M. DOBSON.

Common Cold: Fact or Fancy?

SIR,—In reply to my colleague Dr. David Wheatley (*Journal*, March 1, p. 521), I wish to dispute the insinuation that non-smokers are less likely to succumb to the common cold. Indeed, the converse may be the case. For 16 years I was a confirmed pipe-smoker and then for five years desisted entirely from smoking. During these two periods I noticed no difference in the frequency of my attacks of coryza. For the past three years I have been a heavy smoker of cigarettes and have been astounded at my freedom from colds.—I am, etc.,

Hanworth, Middlesex. B. M. D. ROSTEN.

SIR,—Dr. David Wheatley's experience (*Journal*, March 1, p. 521) is not unique. Three years ago I became a little alarmed by what I hoped was my "smoker's cough" and gave up smoking. I was pleased to find that the cough disappeared rapidly, and surprised and delighted to find that the colds from which I had suffered for as long as I could remember had also gone. For two and a half years I was free from colds. However, nine months ago I started smoking an occasional small cigar, and with the cigars have returned occasional colds. I have no doubt that this is an allergic response to tobacco, and I am now glumly considering giving up the cigars.—I am, etc.,

Lisburn, N. Ireland. ERIC GAREH.

Obituary

E. S. CRISPIN, C.B.E., M.R.C.S., L.R.C.P.

Dr. E. S. Crispin, formerly director of the medical department of the Sudan Government, died at sea, on board the liner *Warwick Castle*, on March 12. He was 83 years of age.

Edward Smyth Crispin was born in London on December 18, 1874, and was educated at Bradfield College and King's College Hospital. After qualifying in 1898, he held the appointments of house-surgeon at the Royal Free Hospital and at King's College Hospital, and then served as a civil surgeon with the South African Field Force in 1899–1900, being awarded the Queen's medal, with three clasps. For the next twenty years he worked in the Sudan Medical Service, being director from 1915 to 1922. He was also president of the Central Sanitary Board and, later, a member of the Governor-General's council. For his services in the lines of communication of the Darfur expedition he was awarded a medal and clasp, and in 1916 received the Order of the Nile. In the following year he was appointed a member of the commission of inquiry into the public health in Egypt. He was appointed C.B.E. in 1920 for his services in Egypt and the Sudan. Soon after the end of the war he returned to England and lived for a while in London before moving to Beaulieu, in Hampshire. He went back to London during the second world war, in which he played his part as an air raid warden. He finally settled at Rottingdean, Sussex, some ten years ago. His third wife, formerly Joy Gilmore, whom he married in 1938, died five years ago.

H. C. S. writes: I first met Edward Smyth Crispin in 1909 shortly after I had joined what was to become the Sudan Medical Service. He was related to Dame Ethel Smyth, the composer. During the war in South Africa he had been a prisoner of the Boers for several months. At the time his contract as a civil surgeon expired he was one of the first three civilian doctors to be offered an appointment in the Sudan. Following a short leave in England, he arrived in Khartum in February, 1901, and as the administration was still almost an entirely military one he was given the honorary rank of bimbashi in the Egyptian Army. Later on in the same year he volunteered to accompany an expedition that was cutting through the vegetation known as the Sudd that blocked the upper reaches of the Nile, in order to reopen a water passage to Rejaf, about 100 miles from the Uganda border, and was in the south for several months. From 1904, when a civilian medical department came to be formed, Crispin was stationed at Port Sudan during the building of the harbour that was to give direct access to the country, and then in 1909, when a reorganization of the medical department took place, he moved to Khartum as assistant director under the P.M.O. of the Medical Corps of the Egyptian Army. Shortly after the outbreak of the first world war, when British officers were recalled from the Sudan, he was appointed Director, and from 1919 until his retirement in 1922 he was a member of the Governor-General's council.

During the early years of the century a rigid economy had to be enforced in the Sudan, and it was not till 1919 that the medical department was able to increase its personnel in order to take over medical work in the central provinces hitherto administered medically by the Medical Corps of the Egyptian Army. But, in addition, during the last three years of his directorship Crispin was responsible for the initiation of three projects, two of which were to have a profound influence on medical work throughout the country. The first was the provision of a hospital ship on the White Nile which was centred on Malakal and which was appropriately named the *Lady Baker* after the first European woman to introduce any modern forms of medical

treatment into this part of central Africa. Then in 1920 a training school for midwives was established in Omdurman, and at the same time preliminary steps were being taken towards the founding of the Kitchener School of Medicine, which was not formally opened until 1924.

Crispin retired at the early age of 48, shortly after the tragic death of his first wife, and, though he was to live for another 36 years, he never undertook any further active professional work. As an administrator he was quick, methodical, and painstaking. He put the organization of his department on to a sound footing and was instrumental in drawing up regulations for it that stood the test of time. As an individual he was most sociably inclined, an amusing companion, and an excellent host. He died at sea on the journey home from a visit to South Africa.

RUBY OLIVE STERN, M.D.

Dr. Ruby Olive Stern, of Northampton, died suddenly on March 13 at the age of 56. She had been in ill-health intermittently since a serious operation two years ago.

A Londoner, born within the sound of Bow bells, Ruby Olive Stern was educated at Queen's College, Harley Street, and Charing Cross Hospital, graduating M.B., B.S. in 1925; she subsequently proceeded M.D., in pathology, in 1932. After holding a post as demonstrator in the pathological department of Charing Cross Hospital Medical School she worked for some years with Dr. J. G. Greenfield on neuropathology at the National Hospital for Nervous Diseases, Queen Square, publishing a series of original papers in *Brain*, including "The anatomical identity of the Werdnig–Hoffmann and Oppenheim forms of infantile muscular atrophy" (1928), jointly with Dr. Greenfield; "A study of the histopathology of tabes dorsalis with special reference to Richter's theory of its pathogenesis" (1929); and "Certain pathological aspects of neurosyphilis" (1932). She became Sebag Montefiore research fellow and morbid anatomist to the Hospital for Sick Children, Great Ormond Street, and two years later was appointed pathologist to St. Andrew's (Mental) Hospital, Northampton. A member of the B.M.A. from the year she graduated, Dr. Stern was for a time assistant secretary of the Marylebone Division.

Dr. Stern married Mr. W. H. Horton, a well-known Northampton manufacturer, and, in deference to his wishes, resigned her appointment at St. Andrew's, though during the second world war she began to work in an honorary capacity in the pathological department of Northampton General Hospital, which she continued to do until comparatively recently, when her health began to fail. In 1954 she published from this hospital in the *British Journal of Cancer* a study of 87 cases of carcinoma of the bronchus, with special reference to solitary cerebral metastases. At the time of her death she was honorary secretary of the local committee of the British Empire Cancer Campaign, and was assisting with the records of the radiotherapy department of the Northampton General Hospital.

Olive Stern had an excellent and well-stored brain, and in the world of neuropathology she had a high reputation, but she gave up the scientific promise of her early years for a happy married life—her husband died three years ago. In her youth she was a skilled musician, and latterly her brilliant personality was constantly seeking for suitable outlets in her adopted town of Northampton. She was a devoted wife and a loyal friend.—R. S. S.

W. E. B. writes: After the war Dr. Stern continued giving freely of her services to the rapidly growing department of pathology at the Northampton General Hospital, and on the inception of the National Health Service the Oxford regional hospital board appointed her honorary consultant pathologist. Her wide practical knowledge of the pathology of the nervous system and of diseases of children was of immense value to and greatly appreciated by her colleagues. A person of a most generous disposition, she devoted much time to aiding a number of worthy causes. Her particular interests in this field were the welfare of animals and the Northampton fund for the British Empire Cancer Campaign. Although in recent years her health had been far from good—she had undergone two major operations in the last five years—she did not permit this to interfere with her work for this cause, and when in hospital for several weeks last year she continued to deal with the secretarial work. Her death has removed from our midst a very gallant woman who bore suffering with great fortitude and who continued to the end to direct all her energies to the benefit of her fellow men.

Sir GEORGE WILSON, C.M.G., M.D., F.R.C.S.Ed. F.R.A.C.S., F.R.C.O.G., F.A.C.S.

Sir George Wilson, honorary consulting gynaecologist to the Adelaide Hospital, South Australia, died recently at Adelaide.

Thomas George Wilson was born at Armidale, New South Wales, in 1876 and was educated at the New England Grammar School and at Sydney University, where he graduated M.B., C.M. in 1899. He then came to the United Kingdom for postgraduate study and took the F.R.C.S.Ed. in 1901. After visits to Vienna and the United States he returned to Adelaide. He proceeded to the M.D. in 1904, and two years later established himself in consultant practice. He had had a very long connexion with the Royal Adelaide Hospital as consulting gynaecologist and with the Queen Victoria Maternity Hospital, Adelaide, as consulting obstetrician, ultimately becoming honorary consultant to both hospitals. He was chairman of the medical board of the Queen Victoria Maternity Hospital from 1916 and president of the board of management from 1936 to 1950. Throughout the first world war he served in various theatres with the Australian Imperial Forces, with the rank of lieutenant-colonel.

After the war Wilson returned to his practice in Adelaide, and in 1925 was appointed director of obstetrics and gynaecology and Edward Willis Way lecturer in Adelaide University, holding both appointments until 1941; but, with the second world war in progress, he continued as acting director until 1944. He was selected a Fellow of the American College of Surgeons in 1924 and a foundation Fellow of the Royal College of Obstetricians and Gynaecologists in 1929. He was a member of the Australian Reference Committee of the Royal College from 1935 to 1947. In 1926 he was elected a foundation Fellow of the Royal Australasian College of Surgeons. He was appointed C.M.G. in 1942 and eight years later created a knight. A member of the British Medical Association for fifty-six years, he was president of the South Australian Branch in 1922–3. He married Elsa M. Cuzens, and had two sons.

FRANK KELLETT, M.B., B.Chir.

Dr. Frank Kellett, director of the Laboratories of Pathology and Public Health and pathologist to the Hospital of St. John and St. Elizabeth, died at the hospital on February 27. He was 55 years of age.

Frank Kellett was born near Dewsbury, Yorkshire, on January 25, 1903. He received his medical education at Christ's College, Cambridge, and St. George's Hospital, qualifying M.R.C.S., L.R.C.P. in 1927. After holding appointments at St. George's Hospital, he joined the Laboratories of Pathology and Public Health in 1928, in which year he took the degrees of M.B., B.Chir., and was appointed pathologist to the hospital of St. John and St. Elizabeth in 1931, remaining with both until his untimely death. He was a member of Gray's Inn.

H. S. W. writes: Frank Kellett was a pathologist of wide experience and high technical skill, and his unexpected death is a great loss to the medical profession. He was a true enthusiast, willing to take endless pains to assist the clinicians in solving the diagnostic problems that so frequently arise.

His insistence on rigorous technique and checking of results went a long way to establish the reputation for reliability that was one of his most marked characteristics. As a friend and colleague, Frank Kellett, with his characteristic sense of responsibility, was invariably loyal and helpful. He possessed a strong sense of humour and a sharp wit which he directed against the follies and pomposities of the world. Although in ill-health for the last few years, he steadfastly continued with his work until within a short time of his death. The deepest sympathy goes to his wife and son and to his mother.

H. CODDINGTON BROWN, C.I.E., M.B., B.Ch. D.T.M.&H.

Major H. Coddington Brown, who was in the Indian Medical Service before becoming bacteriologist to the Wellcome Bureau of Scientific Research, died at the Royal Devon and Exeter Hospital on March 18, aged 81.

Henry Coddington Brown was born on October 28, 1876. He studied medicine at Cambridge and at St. Thomas's Hospital, graduating M.B., B.Ch. in 1902. He joined the Indian Medical Service very shortly afterwards and worked as a bacteriologist in that service. He took the D.T.M. & H. in 1909. He resigned from the I.M.S. in 1919, having been for some time assistant director of the Central Research Institute at Kasauli. A short time before his retirement he was awarded the C.I.E. Having returned to England, Major Brown was appointed bacteriologist to the Wellcome Bureau of Scientific Research, and in the next twenty years or so he published accounts of his research work in both specialist and general medical journals. In 1925 he was one of the authors of a paper on spirochaetal jaundice in Great Britain, and a year or two earlier he had written in this *Journal* about the amoebicidal action of conessine. He retired during the second world war and went to live in Budleigh Salterton.

We are indebted to Sir RICKARD CHRISTOPHERS for the following appreciation: Major Henry Coddington Brown joined the Indian Medical Service in 1902. He was in the same "batch" as myself, and it was during the few months the batch spent in London and Netley that he got the nickname "Cat" Brown in distinction from two other Browns in our batch, and it was by this name that he was for long familiarly known among his special friends. In India Brown joined the Bacteriological Department, and from about 1912 for a number of years was assistant director in charge of the serum and vaccine section of the Central Research Institute, Kasauli, and for a time during the first world war acting director as well during a very strenuous period in which the Institute was responsible for many hundreds of thousands of T.A.B. vaccine doses and other requirements for the Forces. After the war, in 1919, Brown retired from the Service to take up a bacteriological research appointment at the Wellcome Bureau, where he worked for many years and made many important contributions to bacteriology, including some very original work on electrophoresis. During our time at Kasauli and later when working in London I saw much of Brown, and in London often saw him at work in his laboratory, admiring greatly his ingenuity in technique. Brown was a most charming person socially and to work with, always cheerful, kindly, and friendly. He had been somewhat of an athlete and was outstanding as a tennis player at the tennis club in Kasauli. His many friends in the Service will be very grieved to hear of his death.

G. C. SWANSON, M.B., Ch.B.

The obituary of Mr. G. C. Swanson was printed in the *Journal* of March 1 (p. 523).

Dr. W. W. MACKINLAY writes from Balfron, Stirlingshire: "There are men and classes of men that stand above the common herd." So said R. L. Stevenson. George Swanson was one of those, a surgeon not only mechanically able, but, more important still, unusually sound in judgment. Since coming to live in this village his wide knowledge and interests, his friendliness, his humanity, his ability, and his wish to talk to rich and poor alike embodied to many all that a doctor, surgeon, specialist, or otherwise should be. He was a fine specimen of a type which, to our loss, may be passing, and it is tragic that his retirement was so short.

Medico-Legal

ABORTION BECAUSE SUICIDE FEARED

DOCTOR SENT FOR TRIAL

On March 17 a coroner's jury at St. Pancras returned a verdict of manslaughter against Dr. Louis Newton, of Shoot-up Hill, London, and the coroner, Sir Bentley Purchase, committed him for trial at the Old Bailey on April 15 (*Daily Telegraph*, March 18). He was granted bail in £50.

On October 24, twelve days after Dr. Newton had given her a paste injection to terminate a pregnancy, Miss Jean Cook, an Australian nurse aged 35, died in the National Temperance Hospital. Miss Cook had been referred to Dr. Newton by Dr. Ellis Stungo, who stated in his evidence that he took the view that her pregnancy should be terminated because of her mental state. He feared she would commit suicide otherwise. A similar opinion was also formed by Dr. Harold Parsons, a psychiatrist, who had seen Miss Cook earlier. The injection of paste was given in Dr. Newton's consulting-room, and when later Miss Cook became ill Dr. Newton arranged for her admission to hospital.

Medical Notes in Parliament

Aliens and the Health Service

Mr. ERIC JOHNSON (Manchester, Blackley, Con.) asked the Minister of Health on March 17 if he would arrange for the annual compilation and publication of statistics to show the value of treatment and other benefits under the Health Service received by aliens. Mr. D. WALKER-SMITH said he did not think the value of such statistics would be such as to justify the effort and expenditure needed for their collection.

In reply to a specific case cited by Sir MALCOLM STODDART-SCOTT (Ripon, Con.) in which a dentist in Yorkshire was alleged to have treated under the Health Service patients from many foreign and Commonwealth countries, Mr. WALKER-SMITH added that he welcomed the opportunity that was to be given him to look at what on the face of it appeared to be an unusual case.

Mr. ANEURIN BEVAN (Ebbw Vale, Lab.) suggested that the most civilized course would be to extend the area of reciprocal agreement. Mr. WALKER-SMITH said they were always anxious to extend the area of reciprocal agreement. The inhibiting factor in the Health Service was the absence of fully corresponding arrangements in oversea countries. He told Mr. JOHN EDEN (Bournemouth, West, Con.) that there was no evidence of any wide-scale abuse of these arrangements. Against the possibility of taking any action they had to weigh the serious inconvenience to which it would expose British residents.

Medical Examination of Immigrants

Captain H. KERBY (Arundel and Shoreham, Con.) asked the Minister on March 18 whether he was aware that the Aliens Orders did not apply to immigrants from British possessions overseas entering Great Britain, that the majority of such immigrants, mostly negro or coloured, had no

medical examination either in their country of origin or on arrival here, and that this uncontrolled immigration was dangerous to public health in Great Britain; and if he would so amend the Aliens Orders as to require all such immigrants to undergo rigorous medical examination at their British port of entry to ensure that they were free before admission from any infectious disease.

Mr. WALKER-SMITH stated that the Aliens Order, 1953, did not apply to British subjects, but the Public Health (Ships and Aircraft) Regulations, 1952, gave wide powers to port medical officers to deal with cases or suspected cases of communicable disease whether in a British subject or an alien arriving in this country. He had at present no evidence of danger to health from immigration of British subjects such as to justify an extension of the existing arrangements.

Move to Prohibit Chinese Eggs

Mr. A. BALDWIN (Leominster, Con.) asked the President of the Board of Trade on March 18 whether, in view of the general complaints made about the quality of imported Chinese eggs, and the fact that there was a surplus of home-produced eggs, he would prohibit further imports. Sir DAVID ECCLES replied "No." These eggs might be imported under open general licence but subject to examination on arrival under the Public Health (Imported Food) Regulations, 1937.

Mr. BALDWIN said that the Medical Officer of Health of Greenwich, where most of these eggs were imported, had been making a series of allegations and was asking for an interview with the Minister of Health on this point. Was it wise or sensible to be importing eggs which had proved to be poisonous when we were quarrelling with Denmark about the export to them of eggs certified and stamped as laid in this country? Sir DAVID ECCLES said he would bring to the attention of the Minister of Health what Mr. Baldwin had said.

Mr. A. BLENKINSOP (Newcastle upon Tyne, East, Lab.) asked him to consider the important reports from public health laboratories on this subject published a few days earlier, and then consider further action in conjunction with the Minister of Health. Sir DAVID ECCLES said that was a matter for the Minister of Health.

Violence on the Screen

Dr. EDITH SUMMERSKILL (Warrington, Lab.) asked the Minister of Health whether he had considered the statement made by spokesmen of the workers in television and the cinema regarding the increasing amount of violence depicted, a copy of which had been sent to him; and what action he proposed to protect the mental health of the public, liable to be endangered by the exhibition of scenes of violence.

Mr. WALKER-SMITH said that he had seen press reports about this. He did not think that any action was called for on his part, but he would watch the position.

British Oxygen Company

Mr. J. RODGERS (Sevenoaks, Con.) asked the President of the Board of Trade on March 21 what action the Government had taken to carry out the recommendations made in the Report of the Monopolies and Restrictive Practices Commission about the supply of oxygen and dissolved acetylene by the British Oxygen Company.

Sir DAVID ECCLES said that the Commission's conclusions and recommendations on this matter were summarized in the Annual Report by the Board of Trade on the operation of the Monopolies and Restrictive Practices Acts, 1948 and 1953. The Government did not propose to take any action on the majority recommendation that steps should be taken to regulate the levels of the British Oxygen Company's prices and profits on oxygen and dissolved acetylene. The other matters on which the Commission made recommendations had been the subject of discussions between the Board of Trade and the company, and the company had at the Board's request given certain undertakings on those points.

Vital Statistics

Smallpox at Liverpool

A Lascar seaman suffering from semi-confluent smallpox in the pustular stage was admitted to the Liverpool Regional Hospital Board's smallpox hospital at New Ferry in the early hours of March 20. He was a member of the crew of the *S.S. Circassia*, which arrived in the Mersey from Bombay about 9 p.m. on March 19. The ship left Bombay on February 27 and called at Karachi on March 1, Aden on March 5, Suez on March 8, and Port Said on March 10. The rash appeared on March 12. On board was a crew of 54 Europeans and 114 Lascars, and there were 276 passengers.

Vaccination of all crew and passengers was begun by the ship's doctor soon after leaving Port Said, and this was completed on arrival in the Mersey. A second Lascar seaman who had been nursing the patient but who had no symptoms was admitted to New Ferry Hospital and detained for observation. A male passenger with a febrile illness was admitted to Fazakerley Hospital, Liverpool. He was found to be suffering from bronchopneumonia and was detained, as were his wife and child. All other passengers were disembarked at Liverpool and left for various destinations. The ship, with all crew aboard, left for Glasgow at 10 a.m. on March 20. It is understood it will there go into dry dock for normal refitting, and that the crew will be accommodated in the Anchor Line hostel before dispersal.

Week Ending March 15

The chief fluctuations in the notifications of infectious diseases in England and Wales during the week ending March 15 were decreases of 525 for measles, from 4,532 to 4,007, 153 for acute pneumonia, from 690 to 537, 65 for whooping-cough, from 620 to 555, and 28 for scarlet fever, from 938 to 910; the only large increase was 119 for dysentery, from 1,068 to 1,187.

The largest decreases in the incidence of measles were 240 in Glamorganshire, from 471 to 231, 92 in Kent, from 249 to 157, 80 in Suffolk, from 145 to 65, 72 in Herefordshire, from 108 to 36, and 70 in London, from 210 to 140; the largest increases were 54 in Devonshire, from 167 to 221, and 50 in Surrey, from 109 to 159. Only small changes were recorded in the local returns of scarlet fever. The largest fall in the number of notifications of whooping-cough was 32 in Warwickshire, from 57 to 25. For the second consecutive week only 1 case of diphtheria was notified. The number of notifications of acute pneumonia declined in most regions; the largest fall was 40 in Yorkshire West Riding, from 98 to 58.

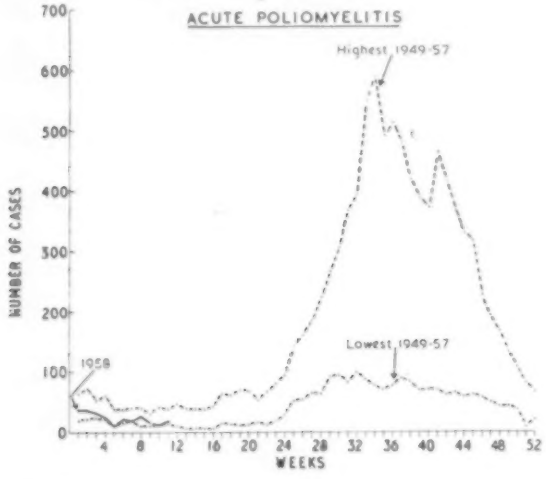
The notifications of acute poliomyelitis numbered 18, and these were 8 more for paralytic and the same number for non-paralytic cases as in the preceding week. The largest return was 6 cases in Buckinghamshire (Newport Pagnell U.D. 4).

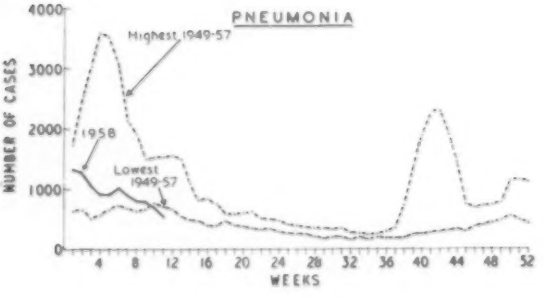
The largest rise in the incidence of dysentery was 70 in Lancashire. The chief centres of infection during the week were Lancashire 399 (Oldham C.B. 143, Liverpool C.B. 66, Manchester C.B. 42, St. Helens C.B. 23, Middleton M.B. 14, Rawtenshall M.B. 10); Yorkshire West Riding 177 (Sheffield C.B. 62, Hemsworth R.D. 32, Leeds C.B. 16, Bradford C.B. 14, Dewsbury C.B. 10); London 117 (Finsbury 19, Fulham 18, Islington 18); Cheshire 90 (Wallasey C.B. 29, Marple U.D. 16); Leicestershire 60 (Castle Donington R.D. 53); Surrey 34 (Kingston-upon-Thames M.B. 15, Carshalton U.D. 14); Warwickshire 30 (Birmingham C.B. 23); Caernarvonshire 28 (Lleyn R.D. 14); Gloucestershire 28 (Bristol C.B. 28); Staffordshire 27; Essex 23 (Thurrock U.D. 11); Middlesex 22.

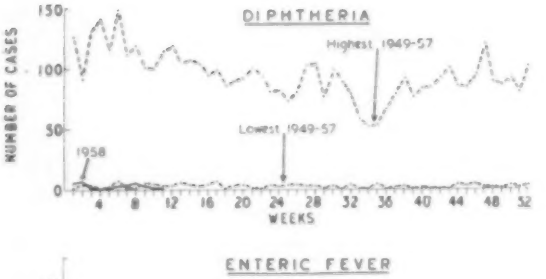
The largest outbreak of food-poisoning was 23 cases in Liverpool C.B.

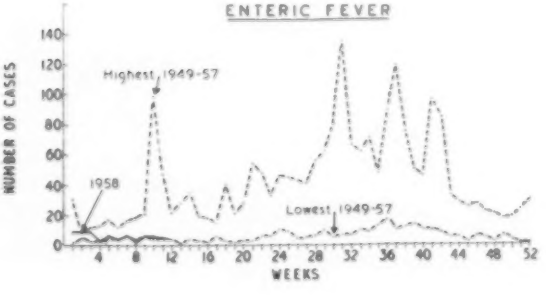
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the years 1949–57 (influenza, 1953–7) are shown thus - - - - - -, the figures for 1958 thus ————. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **March 8** (No. 10) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire	1957 Eng. & Wales	1957 Lond.	1957 Scot.	1957 N. Ire.	1957 Eire
Diphtheria	1	0	1	0	4	6	1	3	0	2
Dysentery	1,068	135	215	7	4	1,214	89	359	10	
Encephalitis, acute	4	0		0		4	0		0	
Enteric fever:										
Typhoid	0	0	0	0	1	1	0	0	0	
Paratyphoid	6	0	0	0	35 (B)	7	1	1 (B)	0	
Food-poisoning	149	21	26	0		151	26	19	1	
Infective enteritis or diarrhoea under 2 years				17	25				8	14
Measles *	4,532	210	95	33	56	24,837	2225	550	407	281
Meningococcal infection	24	2	6	0	1	24	0	14	1	1
Ophthalmia neonatorum	40	2	3	0		37	0	8	0	
Pneumonia †	690	46	355	16	4	206	29	102	10	5
Poliomyelitis, acute:										
Paralytic	5	0	2	0	3	26	1	2	0	7
Non-paralytic	5	0				7	0			
Puerperal fever §	199	34	16	1		206	29	9	1	
Scarlet fever	938	53	101	28	32	837	54	82	56	18
Tuberculosis:										
Respiratory	591	104	87	16		583	72	101	28	
Non-respiratory	78	7	12	3		88	5	17	1	
Whooping-cough	620	38	48	3	16	2,995	189	328	8	54

DEATHS	1958 Eng. & Wales	1958 Lond.	1958 Scot.	1958 N. Ire.	1958 Eire	1957 Eng. & Wales	1957 Lond.	1957 Scot.	1957 N. Ire.	1957 Eire
Diphtheria	0	0	0	0	0	No comparable figures available.	0	0	0	0
Dysentery	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	1	0	0	0	0		0	0	0	2
Influenza	76	1	1	0	0		2	2	1	3
Measles		0	0	0	0		1	1	0	0
Meningococcal infection		0	0				1	0		
Pneumonia	722	64	37	14			62	29	10	9
Poliomyelitis, acute	0	0		0	0		0		0	1
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	102	13	11	4	2		8	11	0	5
Non-respiratory		2	0	0	1		0	1	0	2
Whooping-cough	0	0	0	0	0		0	0	1	0
Deaths 0–1 year	343	39	17	8	14		27	32	5	17
Deaths (excluding stillbirths)	11,590	929	638	142	183		919	672	112	236
LIVE BIRTHS	15,832	1343	1038	223	356		1212	1031	221	385
STILLBIRTHS	367	39	26				29	31		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

New Chair of Anaesthesia.—At the annual dinner of the Faculty of Anaesthetists of the Royal College of Surgeons on March 19, Dr. FRANKIS T. EVANS, the dean, announced that a chair of anaesthesia in the College had been endowed with a gift of £150,000 from the British Oxygen Company. Dr. R. F. WOOLMER, at present director of the department of anaesthesia of the College, would be its first occupant. The dinner, which was presided over by the dean, marked the tenth anniversary of the Faculty and was attended by a "quantity of the quality," as one speaker put it. Among the guests were Mr. J. A. MALIK, the Soviet Ambassador, the Lord Mayor of London, Sir DENIS TRUSCOTT, the Minister of Health, Mr. D. WALKER-SMITH, M.P., and three Russian surgeons at present on a visit to this country, Professors B. A. PETROV, V. I. PSCHENICHNIKOV, and I. S. ZHUROV. The latter were presented with a book each by Sir JAMES PATERSON ROSS, P.R.C.S., who made a short speech, much of which was in what appeared to be excellent Russian. Professor PETROV replied in English. The toast of the Faculty was proposed by the Minister of Health, who then had to leave for the House of Commons and was unable to hear the dean's reply. "The Guests" were toasted by Dr. G. S. W. ORGANE, and the LORD MAYOR, in acknowledgment, had some amusing digs at the medical profession, culled from his experience as a patient, which greatly entertained his audience.

B.M.A. Film Competition, 1958.—For the purpose of encouraging the production of medical films suitable for addition to the Association's film library, the Council of the B.M.A. offers two prizes of fifty guineas each, with certificates for 16-mm. medical films, to be submitted in open competition. One prize will be for commercial and the other for non-commercial film producers. In addition, awards of merit will be made where appropriate. Competitors will be free to choose their own subjects. The films will be judged by a panel of experts, who will pay special regard to the value of the film to the film library and the likelihood of its frequent use. Only films completed within the two years before September 30, 1958, may be entered for the competition. Further details and entry forms are obtainable from the Secretary, B.M.A. House, Tavistock Square, London, W.C.1, the closing date for receipt of films and entry forms being September 30, 1958.

Medical Film Catalogue.—Imperial Chemical Industries Ltd. has issued a catalogue of some 35 medical films available to "approved medical audiences only." These films will not be loaned to scientific film societies or other lay audiences. In addition there are listed seven films on industrial medicine and first aid, produced originally for the company's own training purposes: these films are suitable for lay audiences. Among the "medical films" there is a series on the technique of anaesthesia made in collaboration with the Westminster Hospital Medical School. No charge is made to borrowers of I.C.I. films except for return carriage by post or passenger train. Further details may be obtained from the I.C.I. Film Library, Imperial Chemical House, Millbank, London, S.W.1.

Sanitation of International Airports.—A W.H.O. expert committee, convened to discuss the sanitation of international airports, held its first meeting in Geneva this month. The chairman was Sir HAROLD WHITTINGHAM, formerly medical director of B.O.A.C. In 1937 2.5 million persons travelled on scheduled flights throughout the world; by 1957 the figure was 90 million. This growth, coupled with the size of modern passenger aircraft, threatens soon to overtax the resources of many international airports. At its first meeting the committee discussed the prevention of diseases carried by food, water, or insects other than those provided for under the W.H.O. International Sanitary Regulations.

New Corticotrophin.—From April 1 standardized preparations of corticotrophin (A.C.T.H.) will be available to all hospitals, but they will not be available for prescription on E.C.10. Corticotrophin given to patients therapeutically is nearly always administered by subcutaneous or intramuscular injection. For this reason the units appearing on the labels will in future be based on potency assays in which the hormone has been given subcutaneously. All such preparations will be marked "Not for Intravenous Use." The dosage, in terms of units, to produce a given effect by subcutaneous or intramuscular injection will therefore be unchanged. Corticotrophin to be given intravenously (mainly for diagnostic tests) will be issued in containers marked "For Intravenous Use Only." With these preparations it will be necessary, because of the new assay procedure, to prescribe in future about three times the number of units that have formerly been used in order to produce the same clinical effect (see annotation at p. 765).

Edinburgh's X-Ray Campaign.—By March 18, 190,000 persons in Edinburgh had had miniature chest films taken. The target is set at 330,000 for the whole month of March, or 80% of the city's population over 14 years of age. Of the 190,000, states the *Scotsman* (March 21), 6,600 (3.5%) were recalled for a large film, and of these about a quarter are referred to a chest clinic for investigation. Of 709 persons so referred 44 had pulmonary tuberculosis needing treatment, but only 20 of them were admitted to hospital. This suggests an incidence of cases needing treatment of the order of about 1 in every 2,000 of those passing through the mass miniature radiography units.

Royal College of Surgeons.—At a council meeting on March 13 Professor CLARENCE CRAFOORD, professor of thoracic surgery at Kungl. Karolinska Mediko-Kirurgiska Institutet, Stockholm, was admitted to the honorary fellowship of the College, and Mr. WILLIAM GISSANE, surgeon-in-chief, Birmingham Accident Hospital, was appointed a Sir Arthur Sims Commonwealth travelling professor to visit Australia in 1959. The period of approved training in recognized hospital posts for candidates for the fellowships in otolaryngology and ophthalmology has been extended from 18 months to two years.

Bristol University.—The council has appointed Dr. R. ST. J. BUXTON to a lectureship in physiology, and Dr. P. T. SMITH as a demonstrator in pathology. Dr. A. F. ROGERS has been promoted to a senior lectureship in physiology.

COMING EVENTS

Auxiliary Royal Army Medical Corps Funds.—Annual general meeting, March 31 at 5 p.m. at 11 Chandos Street, London, W.1.

Fifth and Sixth Bahamas Medical Conferences.—Fifth conference, April 1–12 at the Dolphin Hotel, Nassau; sixth conference, December 1–15. Details from Dr. B. L. FRANK, c/o the Dolphin Hotel.

Radio.—"Man, Mites, and Medicine" in the B.B.C. series "Science Survey," April 11, 6.45 p.m. in Network Three.

Wessex Rahere Club.—Spring dinner at the White Hart Hotel, Salisbury, on April 19. Details from Mr. A. DAUNT BATEMAN, F.R.C.S., 11, the Circus, Bath, Somerset.

Central Council for Health Education.—International seminar, April 22–25, at Froebel Educational Institute, London, for medical officers, health educators, nurses, social workers, and others. Details from the Central Council for Health Education, Tavistock House North, Tavistock Square, London, W.C.1.

First European Postgraduate Congress for German-speaking Physicians.—May 16 to 26, at Montecatini, near Florence. The theme of the congress will be digestive and metabolic disorders. Further details from the congress secretariat, 49/iv, Schwanthaler Strasse, Munich, 15.

Military Medicine and Pharmacy.—20th session of the International Office of Documentation of Military Medicine and Pharmacy, June 8–15, in Liége and Brussels. Open to all medical officers (regular or reserve) in the armed Forces. Details from the secretary-général, Hôpital Militaire, 79, rue Saint-Laurent, Liége, Belgium.

American Goiter Association.—Annual meeting, June 17–19 in San Francisco. Details from Dr. J. C. McCLINTOCK, 149½, Washington Avenue, Albany 10, New York.

Association of Physicians of East Africa.—Conference in Nairobi, June 26–28. Details from Dr. J. M. VAIZEY, P.O. Box 2072, Kampala, Uganda.

Royal Microscopical Society.—Exhibition of photomicrographs, July 23–30 at the Polytechnic, Regent Street, London, W.1. Anyone wishing to exhibit should apply without delay to Mr. R. SETTERINGTON, Royal Microscopical Society, Tavistock House South, Tavistock Square, London, W.C.1.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

British Journal of Pharmacology and Chemotherapy.—Issued quarterly (£4 4s. annually). The new issue, Vol. 13, No. 1, includes :

COMPARATIVE EFFECTS OF CHLORTETRACYCLINE AND CORTISONE ON A LOCAL MONILIAL LESION IN THE MOUSE. F. O'Grady and R. E. M. Thompson.
SENSITIZATION OF THE HEART AND NICTITATING MEMBRANE OF THE CAT TO SYMPATHOMIMETIC AMINES BY ANTIHISTAMINE DRUGS. I. R. Innes.
ASSAY OF THE CAPILLARY ACTION OF FLAVANOID COMPOUNDS IN MICE. Mary F. Lockett and D. A. Jarman.
AN INHIBITORY EFFECT OF ACETYLCHOLINE ON THE RESPONSE OF THE GUINEA-PIG ILEUM TO HISTAMINE. M. Maureen Dale.
THE BIOLOGICAL ACTION OF CHLOROPHENOLS. Muriel E. Farquharson, J. C. Gage, and Jean Northover.
THE ACTION OF NITROPHENOLS ON THE METABOLIC RATE OF RATS. Margaret A. M. Cameron.
ANALGESIC ACTIVITY OF (+)-1-[3-METHYL-4-MORPHOLINO-2:2-DIPHENYL-BUTYRYL]-PYRROLIDINE (R.875) IN STUDENT VOLUNTEERS. D. A. Cahal.
THE URINARY EXCRETION OF ADRENALINE AND NORADRENALINE BY RATS UNDER VARIOUS EXPERIMENTAL CONDITIONS. T. B. B. Crawford and W. Law.
THE RENAL REMOVAL OF INJECTED [^{14}C]HISTAMINE FROM THE BLOOD IN DOGS. S.-E. Lindell and R. W. Schayer.
METABOLISM OF INJECTED [^{14}C]HISTAMINE IN THE KIDNEY OF THE DOG. S.-E. Lindell and R. W. Schayer.
CONTINUOUS RECORDING OF ACID GASTRIC SECRETION IN THE RAT. M. N. Ghosh and H. O. Schild.
THE RELATIONSHIP BETWEEN 5-HYDROXYTRYPTAMINE AND ADENOSINE TRIPHOSPHATE IN BLOOD PLATELETS. G. V. R. Born, G. I. C. Ingram, and R. S. Stacey.
INHIBITION BY VARIOUS SUBSTANCES OF OEDEMA FORMATION IN THE HIND-PAW OF THE RAT INDUCED BY 5-HYDROXYTRYPTAMINE, HISTAMINE, DEXTRAN, EGGWHITE, AND COMPOUND 48/80. J. R. Parratt and G. B. West.
THE ACTION OF ATROPINE ON PANCREATIC SECRETION. L. C. U. Junqueira, Hanna A. Rothschild, and I. Vugman.
SOME EFFECTS OF HISTAMINE IN THE NORMAL AND HAEMOPHILUS PERTUSSIS VACCINATED RAT. D. Bovet, R. Kohn, M. Marotta, and B. Silvestrini.
EFFECTS OF RAUNESCINE AND ISORAUNESCINE ON BEHAVIOUR AND ON THE 5-HYDROXYTRYPTAMINE AND NORADRENALINE CONTENTS OF BRAIN. M. K. Paasonen and P. B. Dews.
FORMATION OF HISTAMINE IN THE KIDNEY OF THE DOG. S.-E. Lindell and R. W. Schayer.
THE ACTION OF DOPAMINE ON THE ARTERIAL BLOOD PRESSURE OF THE GUINEA-PIG. O. Hornykiewicz.
THE INFLUENCE OF CORTISONE AND HYDROCORTISONE ACETATES ON THE COURSE OF *Mycobacterium lepraemurium* INFECTION IN RATS. G. A. H. Buttle, P. F. D'Arcy, and E. M. Howard.
A COMPARISON OF THE PITUITARY INHIBITORY EFFECTS OF PREDNISONE, PREDNISOLONE, AND HYDROCORTISONE. J. R. Hodges and Joan Vernikos.
SOME PHARMACOLOGICAL PROPERTIES OF MUREXINE (UROCANOYLCHOLINE). M. J. Keyl and V. P. Whittaker.
A COMPARISON OF ANTIFIBRILLATORY DRUGS IN THE HEART-LUNG PREPARATION. M. J. Rand and J. M. Walker.

Journal of Clinical Pathology.—Issued six times a year (£4 4s. annually). The new issue, Vol. 11, No. 2, includes :

A STUDY OF SURGICALLY REMOVED SPECIMENS OF BREAST, WITH SPECIAL REFERENCE TO SCLEROSING ADENOSIS. A. T. Sandison.
THE STAINING REACTIONS OF CHORDOMA. T. Crawford.
CONGENITAL TOXOPLASMOSIS. R. D. Montgomery, Barbara Donnison, and Hugh Jolly.
LYMPHADENOPATHY IN TOXOPLASMOSIS. J. K. A. Beverley, J. P. Caley, and A. J. N. Warrack.
PRIMARY MELANOMA OF LEPTOMENINGES. J. Bouton.
TRANSFUSIONAL HAEMOSIDEROSIS SIMULATING HAEMOCHROMATOSIS. J. Trevor Hughes and Leslie H. Truelove.
CEREBRAL THROMBOANGIITIS OBLITERANS. L. Wolman.
PLEOMORPHIC SARCOMA OF THIGH WITH LONG SURVIVAL. D. F. Cappell and J. M. Johnstone.
HAEMANGIO-ENDOTHELIUM OF THE SPLEEN AND LIVER. R. G. Tasker.
A CASE OF WEGENER'S GRANULOMATOSIS. A. M. Thomas.
FACTORS AFFECTING THE RATE OF COUPLING OF BILIRUBIN AND CONJUGATED BILIRUBIN IN THE VAN DER BERGH REACTION. G. H. Lathe and C. R. J. Ruthven.
AMINO-ACIDURIA ACCOMPANYING UNTREATED PERNICIOUS ANAEMIA AND SUB-ACUTE COMBINED DEGENERATION OF THE SPINAL CORD. C. W. Crane, R. A. Hayes, and G. C. de Gruchy.
A SCREENING TEST FOR STEATORRHOEA USING ^{131}I-LABELLED TRIOLEIN. M. Lubran and J. D. Pearson.
A COMPARISON OF DIRECT AND EXTRACTION METHODS FOR THE DETERMINATION OF T-1824 (EVANS BLUE) IN PLASMA AND SERUM. J. F. Murray and J. P. Shillingford.
PLASMA CHROMOGEN AND THE ENDOGENOUS CREATININE CLEARANCE. M. H. Roscoe.
SERUM HEXOSAMINE LEVELS IN HEALTH AND DISEASE. Sara Weiden.
NORMAL FAECAL PORPHYRIN VALUES IN BABIES. W. M. Politzer and I. Kessel.
THE SENSITIVITY OF VARIOUS BACTERIA TO ANTIBIOTICS DURING THE YEARS 1951 TO 1956. G. Giles and Eileen M. Shuttleworth.
TECHNICAL METHODS :
A SIMPLE AND SAFE METHOD FOR DETERMINING THE SENSITIVITY OF TUBERCLE BACILLI TO ANTITUBERCULOUS AGENTS. W. McNaught.
PAPER ELECTROPHORESIS OF URINARY PORPHYRINS. Ninan Verghese.
A CONTAINER FOR HANDLING AND CENTRIFUGING PATHOLOGICAL MATERIAL. C. B. Fisher and A. J. Hogan.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Tuesday, April 1

B.B.C. TELEVISION.—9.30 p.m., "Your Life in Their Hands." No. 8. The Fires of Life, from The Western Infirmary, Glasgow.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Professor F. C. Ormerod: Pathology of Internal Ear.
NORTHAMPTON MEDICAL SOCIETY.—At Northampton General Hospital, 8 for 8.15 p.m., annual general meeting. 8.45 p.m., Mr. R. O. Lee: Problem of Venous Thrombosis and Pulmonary Embolism.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. E. H. Larkin: Physical Treatment of Psychiatry.

Wednesday, April 2

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Dr. I. Friedmann, Dr. D. A. Osborn, and Dr. S. Epstein: clinico-pathological conferences.
INSTITUTE OF PSYCHIATRY.—4.30 p.m., public lecture by Dr. H. I. Weinstock (New York): Statistical Evaluation in Psychoanalysis.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Mr. A. W. Badenoch: Haematuria.
MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 8.15 p.m., annual general meeting. Valedictory Address by Mr. Hugh Carson: Hospital Developments.

Saturday, April 5

MIDLAND THORACIC SOCIETY.—Visit to Knightwick Sanatorium, near Worcester, for clinical meeting and annual general meeting.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Silver.—On March 23, 1958, to Jill, wife of Dr. Trevor Silver, a daughter.

DEATHS

Blakely.—On March 11, 1958, at 17, Princes Crescent, Hove, Sussex, Sydney Herbert George Blakely, M.D., formerly of Bedford and Belfast, aged 82.
Bradsworth.—On March 9, 1958, at Birmingham Accident Hospital, Colin Charles Bradsworth, M.B., Ch.B.
Brash.—On March 13, 1958, at Redwick House, Uffington Road, London, N.W., John Walker Brash, M.R.C.S., L.R.C.P.
Brown.—On March 5, 1958, at Victoria Hospital, Kirkcaldy, Archibald Donald Brown, M.B., Ch.B., of Glencairn, Milton Road, Windygates, Fife, aged 63.
Davies.—On March 8, 1958, at Llandough Hospital, David Arwyn Davies, M.R.C.S., L.R.C.P., J.P., of 27, Long Acre Road, Carmarthen.
Elliot.—On February 28, 1958, at Duns, Berwicks, Walter Hutchison Elliot, M.B., Ch.B., of "Morelands," Duns.
Godkin.—On February 27, 1958, at Bouley Bay Lodge, Trinity, Jersey, Channel Islands, Samuel Robert Godkin, D.S.O., F.R.C.S.I., Colonel, I.M.S., retired.
Grierson.—On March 3, 1958, at Fulbeck House, Fulbeck, Lincs, George Arthur Grierson, O.B.E., M.B., C.M., aged 94.
Hancock.—On March 3, 1958, at the Grey House, Barton, Torquay, Devon, Arthur Ernest Hancock, M.R.C.S., L.R.C.P., formerly of Highfield Road, Saltley, Birmingham.
Horton.—On March 13, 1958, at 7, Park Avenue North, Northampton, Ruby Olive Horton (formerly Stern), M.D.
Janney.—On March 4, 1958, Benjamin André Janney, M.R.C.S., L.R.C.P.
Kellett.—On February 27, 1958, Frank Kellett, M.B., B.Ch., of Thames Bank, Taplow, Bucks, and 6, Harley Street, London, W., aged 55.
McCaldin.—On March 12, 1958, Hugh David Cecil McCaldin, M.B., B.Ch., B.D.S., of Fairview Park, Derriaghy, and 239, Lisburn Road, Belfast.
McCann.—On March 13, 1958, at his home, 19, The Grove, Finchley, London, N., Henry Joseph McCann, M.B., B.Ch., aged 55.
Menzies.—On February 27, 1958, at 25, Castle Terrace, Edinburgh, William Menzies, M.B., Ch.B., J.P.
Moon.—On February 26, 1958, at Berrynarbor, Peasmarsh, Sussex, Robert Henry Moon, M.R.C.S., L.R.C.P., of West Norwood, London, S.E.
Russell.—On March 22, 1958, at his home, Hazelwood, Bridge of Allan, Stirlingshire, Sir Alexander James Hutchison Russell, C.B.E., M.D., LL.D., D.P.H., D.T.M., Colonel, I.M.S., retired, aged 75.
Sharples.—On March 12, 1958, at Long Lane, Hermitage, Berks, Joseph Percival Sharples, M.R.C.S., L.R.C.P., formerly of Wye, Kent, aged 87.
Shaw.—On February 28, 1958, in hospital, Ada Shaw (formerly Aspinall), L.M.S.S.A., of Holy Trinity Vicarage, Waterhead, Oldham, Lancs.
Williams.—On February 26, 1958, in London, Thomas Buckley Williams, M.B., Ch.B., J.P., formerly of Croft House, Stalybridge, Cheshire.
Williamson.—On March 5, 1958, Maurice Joseph Williamson, M.C., M.B., Ch.B., Brigadier, late R.A.M.C., retired, of 3, Compton Drive, Parkstone, Dorset, aged 72.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Response to Polio Vaccine

Q.—*A child received a first dose of poliomyelitis vaccine a year ago. Would a second dose now suffice, or should she have two more doses?*

A.—This raises the question of what is the optimum number of injections of polio vaccine and also that of the effect upon the response of the duration of the interval between doses. Neither has yet been fully explored by direct experiment, and therefore one must draw on an analogy between immunization against poliomyelitis and that against other infections.

The antibody response to a first dose of polio vaccine depends partly on the antigenicity of the vaccine but also upon each person's previous experience of natural infections with polio virus. Thus, if a person has had an infection before immunization as shown by the presence of antibodies against one or more types of polio virus in the serum, the vaccine will induce a much larger antibody response (booster effect) than that obtained in a child or adult who has never been exposed to polio virus antigen before, and in whom the vaccine constitutes a primary antigenic stimulus. On the other hand, the second dose of polio vaccine constitutes a secondary antigenic stimulus even in those in whom there is no antibody present before the first dose. In consequence a greater response occurs to the second dose than to the first dose in such persons, whereas the second dose has a relatively smaller effect in those who had antibody present before immunization began.

The answer to the question asked depends upon whether a child loses the booster response to a second injection of vaccine if the interval between the first and second doses is unusually long. There seems no *a priori* reason why this should be the case, and one would therefore expect a second dose of vaccine given after a year's interval to produce a booster effect. On the other hand, a third dose of vaccine is known to produce little further antibody unless the interval between the second and third doses is a long one. One would therefore advise a second dose to be given now and a third dose in a year's time if supplies permit.

Rupture of Long Head of Biceps

Q.—*Is it possible to repair a rupture of the long head of the biceps?*

A.—It is usually possible to repair a rupture of the long head of the biceps. Though possible, such an operation is not always wise. The tendon often ruptures either at its attachment to the glenoid, or at the upper lip of the bicipital groove, and suture at either of these two sites may be followed by a second rupture. For that reason most orthopaedic surgeons prefer to transplant the ruptured tendon, taking it along the course of the tendon of the *short* head of the biceps, and fixing it to the coracoid process of the scapula. This transplant operation gives very good results, and can be recommended with confidence.

Stereotactic Operation

Q.—*What is a stereotactic operation, and what is its therapeutic object?*

A.—A stereotactic operation is a procedure designed to place a lesion accurately in a selected part of the central nervous system. The lesion can be made chemically, as by the injection of alcohol or by electrical methods. To place the lesion accurately a stereotactic apparatus is used, the prototype of this being the Horsley-Clarke apparatus, which has been used for many years in placing lesions in the brains of experimental animals. The object of such an operation is to improve disordered neurological function by producing a destructive lesion in an appropriate part of the brain and not to influence any specific pathological process. An example of such an operation is chemo-pallidectomy, in which alcohol is injected into the globus pallidus with the object of reducing the tremor of Parkinson's disease or the involuntary movements of choreoathetosis. Such operations are at present in the "experimental" stage, but encouraging results have been reported in selected patients.

Bidets

Q.—*Are bidets to be recommended in the interests of hygiene and personal cleanliness?*

A.—Yes; bidets are to be recommended in the interests of hygiene and personal cleanliness, and from time to time they are so recommended by experts in public health. Nevertheless, one has to admit that the bidet has never achieved real popularity in this country; and although they are to be found in some high-class hotels, and there has in fact been an increase in such installations since the war, the increase is a very small one, and it is difficult to say that any real progress has been made. It is an interesting sociological phenomenon that the bidet is very popular in France, a country which is certainly not ahead of England so far as bathing facilities are concerned. The reason for this would appear to be simply a matter of emphasis.

Benzidine a Carcinogen

Q.—*Is it true that the manufacture of benzidine has been discontinued because it has been found to be carcinogenic? What substitute is recommended for it in the benzidine test for occult blood in the faeces?*

A.—It is true that manufacture of benzidine in Great Britain has been discontinued because it has been found to be carcinogenic. The evidence for this is partly clinical and partly experimental. Kennaway, in his original study of carcinogenic coal-tar derivatives in 1924,[1] exonerated benzidine from having any carcinogenic properties, and it was not until 1934 that a paper was published[2] indicating that workers in dye works were getting bladder growths, and relating this to benzidine. It was not clear whether it was benzidine itself or some closely allied by-product in its manufacture that was the carcinogen. However, recent work has shown that benzidine itself is carcinogenic, and also that some of the allied by-products are equally carcinogenic. R. K. Baker[3] has reviewed the most recent evidence on this.

In my own laboratory we have been using o-tolidine[4] instead of benzidine. The o-tolidine test is extremely sensitive, and at its maximum sensitivity gives far too many positive tests in faeces, but it is quite easy to standardize the test to any degree of sensitivity that is required. We have found o-tolidine to give readily reproducible results, whereas the sensitivity of benzidine varies from batch to batch.

REFERENCES
1. Kennaway, E. L., *Brit. med. J.*, 1924, **1**, 564.
2. Gehrmann, G. H., *J. Urol.*, 1934, **31**, 126.
3. Baker, R. K., *Cancer Res.*, 1953, **13**, 137.
4. Kohn, J., and O'Kelly, T., *J. clin. Path.*, 1955, **8**, 249.

Lead Sulphide in Hair-dressings

Q.—*Is the sale of hair-dressings which contain lead and sulphur forming lead sulphide prohibited by law in this country? Is lead sulphide in the form of pomade or liquid dangerous to health because of absorption from the scalp?*

A.—There is no legal control over the sale of lead hair preparations in Britain. Lead acetate preparations above a certain strength are legal poisons, but lead sulphide is not restricted. The main purpose of these preparations is to darken grey or greying hair, and they are sometimes advertised to the public. No cases have been reported in which

lead poisoning has occurred, though claims have been made because unwanted colours have been produced. Lead salts are poisonous wholly or partly because they combine with -SH groups, but this lead sulphide cannot do. Probably a lead preparation is safer than paraphenylene diamine preparations, which are a frequent cause of toxic skin reactions. Chronic lead poisoning is diagnosed largely on blood changes, among which anaemia and punctate basophilia are well known. When lead is absorbed it is deposited in the bones, from which it can be removed by injections of parathormone.

Aetiology of Scleroderma

Q.—*What is known about the aetiology of scleroderma?*

A.—Little is known about the aetiology of scleroderma, and there is in consequence no rational or effective therapy. Much confusion exists on terminology. Scleroderma proper is entirely limited to the skin and is commonly localized (morphoea). Clinically it is related to leucoderma and melanoderma and to alopecia areata, and is probably subject to similar aetiological influences. Systemic sclerosis (acrosclerosis) is sometimes referred to as scleroderma—even to the extent of describing a "scleroderma kidney" and "scleroderma liver," etc. Any and all organs may be involved, but, whereas scleroderma proper is essentially a disease of collagen, is proliferative, and is reversible, the systemic sclerosis is probably secondary to vascular disease, arteriolitis. It is a degenerative, progressive, and atrophic disorder, irreversible, and commonly carries a bad prognosis.

Benzhexol and Nausea

Q.—*Is there any means of overcoming severe nausea caused by benzhexol, which is proving effective in relieving tremor in a case of paralysis agitans?*

A.—Probably the best method of dealing with the severe nausea would be to try diphenhydramine ("benadryl") instead of benzhexol. Diphenhydramine is a substance which prevents nausea, and, since it is also effective in controlling tremor in paralysis agitans, it should solve the difficulty. The other possibility is to reduce the dose of benzhexol and to give diphenhydramine as well. The two together should relieve the tremor and not cause nausea.

Hypothyroidism from Hexyl Resorcinol

Q.—*Is there any risk of hypothyroidism resulting from absorption of hexyl resorcinol from contraceptive pastes which contain this substance?*

A.—Resorcinol may produce hypothyroidism if it is applied to large areas of broken skin in concentrations of about 12% over long periods of time. Hexyl resorcinol is used in much lower concentrations. It immobilizes spermatozoa in concentrations of 0.015%, and is liable to cause irritation in concentrations greater than 0.1%. It is a poorly absorbed substance and there is no evidence that it produces hypothyroidism after absorption. There is thus no risk of diminution of thyroid function from its use as a contraceptive.

Maternal Anaemia and Foetal Anoxia

Q.—*Does anaemia of pregnancy increase the risk of foetal anoxia, and, if so, what degree of anaemia is considered dangerous?*

A.—Maternal anaemia can certainly cause foetal anoxia. In one case a foetus died *in utero* at the 34th week of pregnancy as a result of the mother suffering repeated epistaxis which, during 48 hours, lowered her haemoglobin level from 90% to 30%. This sort of dramatic example, although rare, is convincing. In practice, the anaemia mostly seen during pregnancy is of a chronic variety, and the picture is often confused by a general deficiency state and other forms of ill-health. Although I have not found clear statistical evidence that chronic anaemia by itself causes a higher foetal loss, it is reasonable to assume that it is one factor which operates to cause the higher stillbirth and neonatal death rates known to occur amongst the lower economic and social grades of the community.

The effect of maternal anaemia on the foetus may well vary with the speed at which the state develops and on whether the foetus and placenta can adapt themselves if given the time. The efficiency of the placenta and its reserves of function in any particular case must therefore also influence the development of foetal anoxia. It may be that the effect of maternal anaemia also varies with the period of pregnancy, being least in mid-pregnancy when there is a high proportion of foetal haemoglobin, and most in late pregnancy when foetal haemoglobin is replaced by the adult form and when placental function becomes relatively inefficient. There are so many variables that it is impossible to express the risk precisely in relation to maternal haemoglobin values.

NOTES AND COMMENTS

Butane Stoves.—Dr. F. E. CAMPS and Mr. F. C. SMITH (London) write: In "Any Questions?" (*Journal*, January 18, p. 173) there was an answer to a query about risk of "calor-gas" in caravans. Reading this answer, we feel that it gives a false idea, although, of course, it is correct. The impression that we and several other people have obtained is that it might be interpreted that a caravan would be safe provided the doors and windows were not artificially sealed. This is not, however, quite correct, and if not clarified might, we think, lead to a fatality. We feel that the following quotation probably summarizes the position best: "*Partial combustion of inflammable substances other than coal-gas.* Fatalities from carbon monoxide poisoning are reported each year in cabin cruisers and caravans. These are due to partial combustion caused by inadequate air-changes in small rooms heated by 'calor-gas' or paraffin stoves. Calor-gas itself contains no appreciable quantity of carbon monoxide, but its incomplete combustion is similar to that of paraffin in an ordinary oil-stove in a confined space, carbon monoxide being produced in both cases."[1]

REFERENCE

1 Camps, F. E., and Purchase, W. B., *Practical Forensic Medicine*, 1956, p. 396. London.

OUR EXPERT replies: Partial combustion is a somewhat ambiguous phrase, and may mean either the escape of a proportion of the gas unburned, or the partial oxidation of the gas. The escape of unburned butane does not produce a poisonous atmosphere, although it may produce an explosive mixture. Incomplete oxidation of butane does produce carbon monoxide. Such incomplete oxidation is due to an inadequate admixture of air with the gas before combustion, or to an inadequate supply of air to the flame itself. Both these defects arise from faulty design, or from clogging of air holes, improper adjustment of gas supply, or various other factors. It is *not* the inadequate air-change in small rooms that causes this incomplete oxidation, although it *is* this poor ventilation that allows the accumulation of carbon monoxide, if it is being produced, to toxic levels.

Collected Articles from the "British Medical Journal"

The following books are available through booksellers or from the Publishing Manager, B.M.A. House. Prices, which include postage, are now the same for both inland and overseas.

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Any Questions?, Volumes 2 and 3 (8s. 3d. each).

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